Perinatology Research Branch team at WSU discovers progesterone use dramatically reduces preterm birth rates
As a research university, Wayne State University’s mission is to discover and apply knowledge that contributes to the positive development and well-being of society.

– Dean Valerie M. Parisi, M.D., M.P.H, M.B.A.
Wayne State University

Allan Gilmour
President

Board of Governors

Tina Abbott, Chair
Debbie Dingell, Vice Chair
Eugene Driker
Diane L. Dunaskiss

Allan Gilmour, Ex Officio

Danialle Karmanos
Paul E. Massaron
Annette Miller
Gary Pollard

School of Medicine

Valerie M. Parisi, M.D., M.P.H., M.B.A.
Dean

Jan A. Bertsch, Chair
Julius V. Combs, M.D.
Walter E. Douglas
Gerald D. Fitzgerald
Sidney Goldstein, M.D.
Elizabeth P. Hardy
Taylor A. Lewis, M.D.
Robert J. Lucas, M.D.
Amyre Makupson
Florine Mark
Robert McWhirter, M.D.
Kamran S. Moghissi, M.D.

Jack Ryan, M.D.
A. Paul Schaap, Ph.D.
Kevin J. Sprague, M.D.
Jane R. Thomas, Ph.D.
Irene Walt
In his 1963 appeal on behalf of the United Nations Children's Fund, President John F. Kennedy called children “the world’s most valuable resource and its best hope for the future.”

We owe that most valuable resource the healthiest start possible in life. It is incumbent upon us as a society, as a country, as a university, as physicians and medical researchers that we do everything within our power to ensure that every child is born healthy and given the best possible launch along the path to becoming our best hope.

One can get a sense of just how fragile too many of our children are at birth by visiting a neonatal intensive care unit. Some children are born so early and so small that their bodies can be cupped in the palm of your hand. Several decades ago, these children all perished. Our science has evolved to the point that we can now positively impact both their survival and the quality of their lives.

The Wayne State University School of Medicine is helping the Renaissance City re-invent itself yet again, this time as a national leader of children’s health medical research. In fact, Detroit and Wayne State University are fast becoming known as the research center that took what is likely the greatest leap forward to date in the battle against premature birth. In 2011, the team at the Perinatology Research Branch housed at Wayne State University and the Detroit Medical Center announced that the use of progesterone in mothers identified at risk for premature birth cut that risk nearly in half. That is medicine that we can use, quickly and inexpensively, to dramatically change health factors in the state of Michigan and around the world.

The most recent example of how the PRB advances maternal-fetal medicine was published in the April 2012 edition of the prestigious journal Science Translational Medicine. Researchers demonstrated that a nanotechnology-based drug treatment in newborn rabbits with cerebral palsy enabled dramatic improvement of movement disorders and the inflammatory process of the brain that causes many cases of CP. The findings strongly suggest there may be an opportunity immediately after birth for drug treatment that could minimize CP. The study was the first to show that an anti-inflammatory drug delivered with a nanodevice can dramatically improve CP symptoms in an animal model.

We are engaged in a new level of personalized medicine, one in which science and medicine will treat disease and disability in the womb, at molecular levels only dreamed of in the wildest fancies of science fiction writers. The Wayne State University School of Medicine is leading the way into that new frontier.

We have the treasure of probing minds that allow us to continue to explore the ever-surprising universe that is the human body at minutely detailed levels. But we are only standing at the threshold of a new era of medicine. We must keep probing as we assist in establishing the miraculous as the new standard of care. We owe that to our children, because, as the celebrated theologian Dietrich Bonhoeffer noted, the true test of the morality of a society is what it does for its children.

Valerie M. Parisi, M.D., M.P.H., M.B.A.
Dean
Wayne State University
School of Medicine
Joann Wang, M.D., is working to improve treatments for neuroblastoma, a cancer that affects children. Her research is supported by the Children’s Research Center of Michigan.

The Children’s Crusaders

by Phillip Van Hulle and Andrea Westfall
Photos by David Dalton
Neuroblastoma is a challenging word for young children to pronounce. It’s a word parents hope to never hear.

The word is the name medical science gives the most common form of a malignant solid tumor in childhood cancer outside of tumors of the brain. It is the most common cancer in infants.

The cancer develops in early forming nerve cells of the sympathetic nervous system, and often begins in the abdomen of young children. Parents may not recognize anything is wrong until they find a lump in their child’s abdomen, chest or neck during bathing. If the condition has spread, other indications can include pain in the chest and difficulty breathing, pain in the arms and legs, pain in the back or weakness or paralysis of the legs, according to the American Cancer Society. The ACS reports that about 650 new cases are diagnosed annually in the U.S. In nearly two-thirds of those cases, the disease has metastasized beyond the abdomen.

The Children’s Neuroblastoma Cancer Foundation says the condition affects almost twice as many infants as leukemia. About 70 percent of children diagnosed with neuroblastoma are in the advanced stages of the disease, and less than 40 percent of those live five years beyond diagnosis and treatment.

Neuroblastoma is commonly diagnosed in children younger than age 5, striking one of every 100,000 in the United States. Twenty-five percent of neuroblastoma diagnoses take place in children younger than age 1. If there is any good news related to the disease, it is that children diagnosed younger than age 1 demonstrate a 90 percent cure rate. Treatment options include surgery and chemotherapy, as well as stem cell and bone marrow transplants.

A Wayne State University School of Medicine researcher is working to increase those survival rates by investigating new agents to overcome chemotherapy resistance in neuroblastoma patients.

“Neuroblastoma remains a major therapeutic challenge in Pediatric Oncology despite decades of intensive research and therapeutic trials,” said Joann Wang, M.D., assistant professor of Pediatrics. “With current treatment protocols, including high-dose chemotherapy with autologous stem cell transplantation, radiation and surgery, patients with high-risk metastatic neuroblastoma have long-term survival rates of less than 40 percent. This highlights the chemotherapy-resistant nature of this tumor. Therefore, new agents are urgently needed to overcome chemotherapy resistance so as to improve the treatment outcome of this deadly disease in American children.”

Dr. Wang said her research will lead to the development of novel treatment approaches for children with neuroblastoma by integrating new therapeutic agents such as Histone Deacetylase Inhibitors. The study will establish the molecular mechanisms underlying the synergy between HDACIs and DNA-damaging drugs in neuroblastoma tumor cells, and will provide a “solid foundation” for clinical evaluation of standard chemotherapy drugs in high-risk neuroblastoma. A better understanding of the biological function of individual HDACIs may lead to the development of more effective therapies, including the development of new drug combinations and new rationally designed HDACIs, she said.
William Lyman, Ph.D., director of the Children’s Research Center of Michigan, says the center can provide research grants, lab space and staff to advance research that benefits the population segments of the greater Detroit region.

Developed during the last decade, HDACIs have shown great potential for the treatment of cancer, Dr. Wang said. Recent studies demonstrated that HDACIs can decrease the ability of cancer cells to repair DNA damage by suppressing critical DNA repair genes. She hypothesizes that combining HDACIs with DNA-damaging chemotherapeutic drugs for treating neuroblastoma would result in enhanced anti-tumor activities of the drugs. That hypothesis is strongly supported by her preliminary studies, which show synergistic anti-tumor activities between a novel HDACI and cisplatin, doxorubicin or etoposide, the main drugs used in treating neuroblastoma.

“We all know that genetic instructions used in the development and functioning of human and other living organisms are stored in DNA, which usually exists as a pair of molecules that are held tightly together and entwine like vines in the shape of a double helix,” Dr. Wang explained. “To carry out gene expression, a cell must control the coiling and uncoiling of DNA, a process controlled by Histone deacetylase. HDACIs affect the gene expression in cancer cells, although medical researchers don’t yet know the exact anti-cancer mechanisms.

“Many HDACIs have been identified now and some are to be tried in pediatric cancers, including neuroblastoma,” she said. “Our preliminary data with neuroblastoma cell lines suggest one of the newer HDACIs could be a more effective drug in the treatment of neuroblastoma. We plan to further study how it works and how to use it to develop more effective treatment for the high-risk neuroblastoma.”

That includes the ability to better identify which patients would not respond well to current therapies before treatment begins so that a more effective therapy could be provided.

In 2011, Hyundai Hope on Wheels and the Metro Detroit Hyundai dealers awarded Dr. Wang a $100,000 Hope Grant to fund her research on the treatment of high-risk neuroblastoma.

Dr. Wang said that grant, and her research, would not be possible without the support of the Children’s Research Center of Michigan, which has provided a grant and lab space. Without that support, “I would have had to give up the lab research.”

Founded in 1997, the Children’s Research Center of Michigan is operated by Children’s Hospital of Michigan with the collaboration of the Detroit Medical Center, Wayne State University and the Barbara Ann Karmanos Cancer Institute. The center works to provide a more efficient mechanism for physicians and medical researchers to pursue existing and new medical investigations into
The CRCM brings together the potency of its collaborating entities to further medical science to benefit children, particularly the children of the greater Detroit region, said William Lyman, Ph.D., professor of Psychiatry and Behavioral Neurosciences for the Wayne State University School of Medicine and the Carman and Ann Adams Endowed Chair of Pediatric Research director of the Children’s Research Center of Michigan. The center can provide research grants, lab space and expertise through a staff of biostatisticians. That infrastructure can push research further by providing funding, space and staff that many researchers otherwise would need to procure from scratch to launch a project.

The key criterion for the CRCM to consider a researcher’s application is its impact on the home population. Studies and their findings must be related to populations in the greater Detroit region.

“We can provide grants and infrastructure,” said Dr. Lyman, who also serves as WSU professor and associate chair of Pediatrics for Research, “but the work must go forward with the idea of benefiting the people of the Detroit area. That may be the entire population, the African-American population, the Arab American population or other segments. The research might involve populations in overseas countries, but only as they relate to the people of our region.”

Much of the research, Dr. Lyman said, might not take place, or might not be so advanced, without CRCM support. Individual grants can range from $10,000 to $50,000. The grants are funded by the Children’s Hospital of Michigan Evergreen Endowment, supported by the hospital’s annual Festival of Trees event.

The Children’s Research Center of Michigan also supports Michael Klein, M.D., a pediatric surgeon, in his efforts to develop a smarter scalpel.

Dr. Klein, professor of Surgery and the Arvin I. Philippart, M.D. Endowed Chair in Pediatric Surgical Research and Research in Solid Tumors of Childhood for the Wayne State University School of Medicine, is relying on funding and facilities provided through the center to create a scalpel that can “see” during surgeries to remove cancerous tumors.

The scalpel would incorporate Raman spectroscopy, a technique that identifies the characteristics of objects — including cancerous and healthy human tissue — by their property of scattering light produced by a laser.

During an average tumor removal surgery, the surgeon removes all of the tumor that can be seen. While the patient is still under sedation, samples of the excised tissue are sent to a pathologist, who determines whether the...
surgeon has reached healthy tissue, an indication that the entire tumor has been removed. If the pathologist says cancerous tissue remains, the surgery continues and another sample is sent to the lab. The interval between sending the sample to Pathology and awaiting a response, Dr. Klein said, is about 20 minutes. The process can be repeated two to three times during a surgery. This requires that physicians keep the patient sedated for longer periods, which can open the door to complications. If, however, the surgeon has a scalpel that can indicate when healthy tissue has been reached, the down time between pathologist reports can be eliminated, and the surgery made briefer.

“This would eliminate the wait, speed the surgery, and be better for the patient,” Dr. Klein said.

The process for removing a tumor from the brain can be even more taxing on patients.

“With a brain tumor, you remove what you can of the tumor and then close the patient up,” he said. “The next day you perform an MRI to determine whether you have to go back in (to remove more of the tumor), so complete removal could take two or more separate surgeries.”

Additional surgeries could be eliminated with a scalpel that can tell a surgeon immediately if all cancerous tumors have been removed during the initial procedure.

“We wouldn’t be doing this without the center,” which provided funding and some facilities, Dr. Klein said.

Using similar technology, Dr. Klein, working with researchers at the WSU College of Engineering, also is working on the development of a probe that can identify cancerous tissue without a biopsy.

Such a probe, he said, could be used by dermatologists to determine the malignancy of suspected skin cancers. Now, when a patient with a suspicious skin growth visits a dermatologist, the physician has little choice but to perform a biopsy to determine whether the lesion is malignant or benign. The procedure requires numbing the affected area, shaving off a portion of the lesion for testing, discomfort or pain for the patient when the local anesthetic wears off, followed by 10 to 14 days of anxiety for the patient while awaiting the test results to determine whether the lesion is cancerous and requires treatment. With the probe or wand, Dr. Klein said, the dermatologist could move the device over the suspect area and get an immediate determination, replacing today’s biopsy and the wait for results.

He also is investigating the use of such a probe endoscopically in suspected pancreatic and colon cancer.

Sharada Sarnaik, M.D., a professor of Pediatrics at the WSU School of Medicine, has cared for children living with sickle cell disease for nearly 40 years. She has seen much progress in the area of treatment and care in those four decades, thanks in part to work supported by the CRCM.

The clinician and researcher is director of the Sickle Cell Center, located on the second floor of Children’s Hospital of Michigan. The center, established in 1973, sees about 2,000 patients every year, the majority of whom have the HbSS type of the disease – the most common and most severe form, known as sickle cell anemia. Sickle cell is a painful and debilitating inherited disease that presents itself in infancy, usually at about 5 months old, according to the U.S. Centers for Disease Control and Prevention.

For 30 percent of the center’s patients, many of them infants, the pain is so severe that Dr. Sarnaik and team prescribe a chemotherapy drug called hydroxycarbamide,
or hydroxyurea, proven to significantly reduce pain in infants in a national study co-authored by Dr. Sarnaik and administered through the CRCM.

Hydroxyurea – a mild chemotherapy agent commonly used to treat adults and adolescents with sickle cell anemia – is safe and effective in reducing pain and other complications in infants with the condition. Specifically, the authors concluded that “hydroxycarbamide substantially reduces episodes of pain and acute chest syndrome, admissions to hospital, and transfusions in adults with sickle cell anemia,” according to a May 14, 2011, report in The Lancet. The research was funded by the National Institutes of Health, and said Dr. Sarnaik, may give doctors around the world an effective and inexpensive way to provide pain management for these young patients. Dr. Sarnaik was the principal site investigator for CRCM, one of 13 participating centers.

Those who have the SS type of the disease inherit two sickle cell genes, one from each parent. This form is most common in those of African descent, although it affects people of varying racial and ethnic groups, including descendants of families with ties to South America, Central America, Turkey, India, Asia, the Middle East and the Mediterranean. According to the CDC, the disease occurs in one in every 500 African-American births, compared to one in every 36,000 Hispanic-American births.

“They feel like it originated in Africa but one never really knows,” Dr. Sarnaik said. “The slave trafficking brought the gene to the West here.”

In November 2010, the NIH marked the 100th anniversary of the first published case of sickle cell disease in the U.S. Sickle cell disease can be found at birth during the mandatory newborn screening test shortly after delivery, but can also be diagnosed through a prenatal test. Dr. Sarnaik is a supporter of genetic counseling and genetic testing to facilitate appropriate family planning. “Our city is predominantly African-American, so what needs to happen is an increase (in) awareness,” she said.

In 2010, the most recent figures available, African-American infants accounted for 97 percent of the 61 confirmed cases of sickle cell disorders reported in Michigan, according to the July 2011 Michigan Department of Community Health Newborn Screening Follow-Up Brief on Sickle Cell Disorders in Michigan.

More recently, Dr. Sarnaik has seen a steady rise in local Arab American and Jamaican-American children in the center, something she attributes to an increase in those populations moving to the greater Detroit region.

The sickle cell name comes from the shape...
red blood cells take in its patients. The cells are normally round and easily deliver oxygen from the lungs to other body tissues. In patients with sickle cell disease, the cells are hard, sticky and curved like a sickle tool, clogging blood flow throughout the body and leading to acute pain attacks and acute chest syndrome, stroke and infection.

“The pain is awful,” Dr. Sarnaik said. “It hurts like the dickens and there’s no predicting it. “Treatment can make a difference, though. It is as severe as it always was, but we have more technology and better treatments,” she said, citing the strides in pneumococcal vaccine, stem cell transplants and pain management such as the CRCM study.

With the assistance of the CRCM, Gaurav Kapur, M.D., a pediatric nephrologist at Children’s Hospital of Michigan, is working to isolate kidney stem cells. The ultimate aim of his research is to identify the stem cells so that they may be incorporated into regenerating kidneys and repairing organs damaged by disease.

The associate director of the dialysis program at Children’s Hospital of Michigan, Dr. Kapur said that while his studies are still in the early stages, the research has the potential to assist an increasing number of patients.

“The limited treatment options available to patients with kidney disease, associated with rising health care costs and increasing contribution of kidney disease patients to these costs – $81.4 billion in 2007 – clearly highlight the need for alternative therapeutic modalities,” he said.

According to the National Kidney & Urologic Diseases Information Clearinghouse, chronic kidney disease in 2010 affected 20 million (more than 10 percent of) Americans 20 or older. In 2009, the U.S. Centers for Disease Control and Prevention said 3.9 million Americans (1.7 percent) were diagnosed with kidney disease. That same year, kidney disease killed 48,935 Americans, a rate of 15.9 deaths for every 100,000 people. The CDC ranked kidney disease the ninth leading cause of death in America that year, the last full year for which statistics are available.

The Michigan Department of Community Health ranked kidney disease as the eighth leading cause of death in the state in 2010. Five Michigan residents died of kidney disease every day in 2009.

Renal stem cells are considered capable of self-renewal and differentiation into tissue- or organ-specific cell types, Dr. Kapur said. Therapeutically, he is researching the use of renal stem cells because of their potential for tissue regeneration and repair, which could prove invaluable in treating those with kidney disease.

“The CRCM has been instrumental in the progression of this research,” said Dr. Kapur, who also serves as associate director of the Pediatric Nephrology Fellowship. “Besides using the CRCM lab facilities, I have also received financial support from the CRCM in conducting this research. The research would not have been possible without their support.”
La-Ron Scott is only 1 year old, but his mother, Crystal Thomas of Detroit, said that he’s all boy — obsessed with music and cars. “He loves cars,” Thomas said. “At 12 months old, he’s making sounds like he’s driving a car and I’m like, ‘How can he know what sound a car makes?’”

La-Ron is also happy and healthy, but that may not have been the case if not for the clinical trial that his mother enrolled in at the Perinatology Research Branch at Wayne State University.

Thomas was early in her pregnancy when she began feeling an uncomfortable pressure in her abdomen. Her family physician told her it was likely that she would only be able to carry her baby for seven months, resulting in a premature birth and the potential for an array of lifelong corresponding health problems. Thomas, who is working on her bachelor’s degree in nursing at Wayne State University, was told she would have to go on bed rest.

However, when Thomas went to Hutzel Hospital for an ultrasound to determine the gender of her baby, experts discovered that she had a short cervix, a condition that put her at very high risk for preterm delivery. Her physician, Sonia Hassan, M.D., professor of Obstetrics and Gynecology at the Wayne State University School of Medicine, told her about a clinical trial to prevent premature birth in which women were treated with a placebo or a low-cost bioidentical form of natural progesterone from the mid-trimester of pregnancy until term.

Thomas enrolled in the study and the pressure in her abdomen faded. She did not need to go on bed rest. “Not only did I carry my baby nine months, but I received 3D pictures and ultrasounds of my child,” Thomas said. “It was a miracle for me because I was in school at the time.”

She’s still working on her degree and plans to specialize in pediatrics. “I just love children,” she said. The daily application of progesterone can reduce the rate of preterm delivery by as much as 45 percent in women at high risk for early delivery.
Dr. Hassan, the associate dean for WSU Maternal, Perinatal and Child Health, was the lead author of a groundbreaking clinical study for a new method for preventing premature birth in millions of women each year, published in the medical journal *Ultrasound in Obstetrics & Gynecology*. The study showed that the rate of early preterm delivery in women less than 33 weeks into their pregnancy can be reduced by 45 percent simply by treating the women at risk with a low-cost gel of natural progesterone from mid-trimester until term.

“Our group has been working on this approach to reducing infant mortality for much of the past decade; it’s very exciting to see that the effort is paying off and that mothers and infants will be able to benefit from it,” said Dr. Hassan, director of the Center for Advanced Obstetrical Care & Research within the Perinatology Research Branch at the Wayne State University School of Medicine and a recognized authority in the study of the uterine cervix during pregnancy.

The peer-reviewed research and findings were led by the Perinatology Research Branch of the National Institutes of Health, housed at the Wayne State University School of Medicine and Hutzel Women’s Hospital in Detroit. The findings in “Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial” will have substantial impact on the practice of medicine, said the lead author of the three-year clinical trial.

“This study offers hope to women, families and children,” Dr. Hassan said. “Worldwide, more than 12 million premature babies — 500,000 of them in this country — are born each year, and the results are often tragic. Our clinical study clearly shows that it is possible to identify women at risk and reduce the rate of preterm delivery by nearly half, simply by...
treating women who have a short cervix with a natural hormone — progesterone.”

Dr. Hassan also pointed out that numerous studies — many conducted by the Perinatology Research Branch — over the past decade have shown that ultrasound of the uterine cervix can identify pregnant women who are at high risk for preterm delivery. The ultrasound examination is simple to perform, painless and can be performed between the 19th and 24th weeks of pregnancy. Pregnant women with a short cervix (one that is less than 25 millimeters long) are at very high risk for preterm delivery.

Once a mother at high risk for preterm delivery has been identified she can be offered treatment with the progesterone gel. The inexpensive gel is applied by the mother intravaginally daily. Generally, women are identified as high risk between 19 and 24 weeks of gestation. They apply the progesterone through the 37th week of pregnancy. Of major interest is that progesterone reduced the risk of preterm delivery not only at less than 33 weeks gestation, but also at less than 28 weeks and less than 35 weeks (secondary endpoints of the study). It also reduced the rate of respiratory distress syndrome, the most common complication in premature babies.

“The findings of the study are especially good news for expectant mothers in Detroit,” said Dr. Hassan, a native of Michigan. “Preterm delivery has long been a major health care problem in the city.”

In 2008, more than 17 percent of births in Detroit were premature, and they accounted for more than 70 percent of the infant mortality recorded in that year, according to the latest research from the Michigan Chapter of the March of Dimes.

The city’s high infant mortality rate, preterm delivery rate, and ethnic and racial disparity in birth outcomes were important considerations in the National Institutes of Health’s decision to establish the Perinatology Research Branch in Detroit 10 years ago. The branch allows women in the region to obtain state-of-the-art medical care and join medical studies to improve prenatal diagnosis, monitor fetal growth, predict preeclampsia and prevent premature birth and the potential lifelong difficulties that attend it.

Describing the results, which showed that the rate of preterm birth among women with a short cervix had been reduced by 45 percent, Dr. Hassan, director of the Wayne State/Perinatology Research Branch/Detroit Medical Center Maternal-Fetal Medicine Fellowship Program, noted in the study: “The main implication for clinical practice is that universal screening of women with ultrasound examination in the mid-trimester to identify patients at risk (based on a short cervix) can now be coupled with an intervention — the administration of vaginal progesterone — to reduce the frequency of preterm birth and improve neonatal outcome. This can be accomplished conveniently.

“We’re obviously very gratified by these results,” Dr. Hassan said. “Based on the findings of our clinical trial, we expect that obstetricians and clinicians will provide expectant mothers with ultrasound screening for cervical length, and to make progesterone therapy available to those who present with a short cervix.”

The study was conducted at 44 centers worldwide during the past three years, and included patients from the United States, South America, Europe, Asia and Africa, and screened more than 32,000 women for a short cervix.

Subsequent findings based on an individual patient meta-analysis of all randomized clinical trials of vaginal progesterone conducted worldwide include:
The vaginal application of progesterone reduces the rate of preterm birth in women at less than 33 weeks of gestation, but also is effective at less than 28, 32 and 35 weeks. Vaginal progesterone reduces both “early” and “late” preterm births. Early preterm births (less than 32 weeks) are associated with a high rate of neonatal complications and long-term neurologic disability. Late preterm births (34-36 6/7 weeks) represent 70 percent of all preterm births, and although they have a lower rate of complications they are still a major health care problem.

Vaginal progesterone was effective in women with a short cervix and who had or had not previously given birth prematurely.

The benefits of progesterone administration were observed in women who had a cervical length of 25 mm or less.

This was the first study to show that vaginal progesterone is effective in reducing the rate of neonatal complications in twin gestations. Previous studies of natural and synthetic progestins have been negative. This study found that progesterone benefits women with a twin gestation and a short cervix.

There was remarkable consistency of the magnitude of the effect of vaginal progesterone in the prevention of preterm birth among studies conducted in different parts of the world.

The results indicate that it is now possible to offer all pregnant women a method to determine whether they are at risk for preterm

Pregnant women with a short cervix (one that is less than 25 millimeters long) are at very high risk for preterm delivery. Dr. Sonia Hassan says an ultrasound examination is simple to perform, painless and can be performed between the 19th and 24th weeks of pregnancy.

Vaginal progesterone administration to women with a short cervix detected by ultrasound reduced the rate of admission to newborn intensive care units; respiratory distress syndrome; the need for mechanical ventilation; and a composite score of complications that included intracranial hemorrhage, bowel problems, respiratory difficulties, infection and death.
birth and prevent a significant number of preterm births in women with a short cervix using vaginal progesterone.

Universal implementation of cervical ultrasound and vaginal progesterone is estimated to result in the prevention of approximately 30,000 preterm births at less than 35 weeks in the U.S. per year, with an annual savings of more than $500 million in health care costs.

“The results of this study provide compelling evidence that vaginal progesterone administration to women with a short cervix is an effective strategy to reduce preterm birth,” said Valerie M. Parisi, M.D., M.P.H., M.B.A., dean of the WSU School of Medicine. “This study indicates that to prevent one case of preterm birth at less than 33 weeks of gestation, only 13 mothers with a short cervix would need to be treated, and 11 to prevent one preterm birth at less than 35 weeks of gestation. This makes progesterone the most powerful strategy to reduce preterm birth developed thus far.”

“As a research university, Wayne State University’s mission is to discover and apply knowledge that contributes to the positive development and well-being of society,” Dean Parisi said. “These findings are an example of research that is quickly translated into improved clinical care outcomes. Wayne State will aggressively share this new knowledge with health care providers here in Detroit, in Michigan and around the world so that it can benefit pregnant women. I’m confident that the strong partnership between the PRB, the Detroit Medical Center and Wayne State will continue to result in pioneering contributions for pregnant women and unborn children.”

Dean Parisi, as a keynote speaker, announced and recommended universal cervical ultrasound and progesterone therapy at the Michigan’s Call to Action to Reduce and Prevent Infant Mortality Summit on Oct. 17, 2010. The summit, called for and hosted by Gov. Rick Snyder, attracted hundreds of physicians, caregivers and stakeholders with a role in reducing the state’s high infant mortality rate. After the presentations by Dean Parisi, Lawrence Reynolds, M.D., president and CEO of Mott Children’s Medical Center, and Mouhanad Hammami, M.D., chief of Health Operations for the Wayne County Department of Health and Human Services, the attendees broke into work groups for a day-long planning session to develop best recommendations to attack the problem. The planning groups advised that the state quickly adopt the interventions Dean Parisi recommended, including establishing universal cervical length screening and the use of progesterone for the prevention of preterm birth.

The first immediate clinical intervention Dean Parisi recommended is statewide ultrasound screening of pregnant women for a shortened cervix. If a woman is found to have a short cervix, she can be treated with vaginal progesterone, which is available by prescription.

Adopting universal cervical length screening using ultrasound would require ensuring regional access to the necessary equipment, providing diagnostic training and providing insurance coverage for screenings. Statewide universal ultrasound screening, Dean Parisi said, would be cost effective. With Michigan’s 110,000 births annually, the potential cost savings has been estimated to be $19,603,380 (in 2010 dollars) for every 100,000 women screened.
Wayne State University and the Perinatology Research Branch lead the way in the fight against preterm birth
Every mother deserves a healthy baby and every baby deserves a fighting chance. That’s the underlying philosophy of the researchers at the Perinatology Research Branch of the National Institutes of Health, housed at the Wayne State University School of Medicine.

The Perinatology Research Branch, the only center of its kind in the nation, is a component of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) of the National Institutes of Health (NIH). The mission of the NICHD is to ensure that every baby is born healthy and wanted and that women suffer no harmful effects from pregnancy. This mission is enacted by conducting clinical and laboratory research to understand the complications of pregnancy and develop methods for the early diagnosis, treatment and prevention of these complications.

Brought to the Wayne State University School of Medicine in 2002 through a 10-year contract with the National Institutes of Health, the Perinatology Research Branch also serves as a major hub for the development and training of physicians and scientists who have pioneered diagnostic tests and treatments in maternal-fetal medicine.

The Perinatology Research Branch is strategically located to serve a high-risk population that requires the full spectrum of services the branch offers, including the most advanced three-dimensional and four-dimensional ultrasound for prenatal diagnosis. Since locating at the Wayne State University School of Medicine and the Detroit Medical Center at Hutzel Women’s Hospital, the branch has assisted more than 20,000 at-risk mothers, most of them uninsured.

There clearly is a critical need, locally and worldwide, for the services and medical research conducted at the Perinatology Research Branch.

In 2005, nearly 13 million babies — about 10 percent of births worldwide — were born preterm, or before 37 weeks gestation. “The Global and Regional Toll of Preterm Birth,” a report released by the March of Dimes in late 2009, declared that about 1 million deaths in the first month of life, or 28 percent of newborn deaths around the world, could be traced to a complication from premature birth. While the majority of women (11 million) giving birth prematurely did so in Africa and Asia, the United States and Canada recorded a combined 500,000 premature births. Since the report counted only single births and mothers with no known medical conditions, it is likely the data underestimated the severity of the problem.

Data compiled by the World Health Organization and used for the 2009 March of Dimes report indicated that 10.6 percent of births in North America (the United States and Canada) are premature, second only to the 11.9 percent rate of Africa. In the United States, premature births have increased 35 percent in the last quarter century.

Babies who do survive preterm birth face a life filled with a litany of health risks, including cerebral palsy, blindness and learning disabilities. “Premature births are an enormous global problem that is exacting a huge toll emotionally, physically, and financially on families, medical systems and economies,” Jennifer L. Howse, president of the March of Dimes, said in a statement upon the release of the global report. “In the United States alone, the annual cost of caring for preterm babies and their associated health problems tops $26 billion annually.”

Wherever trend data are available, according to the March of Dimes, the rates of preterm birth are increasing around the world. In fact, the U.S. consistently records higher infant mortality rates than most other developed countries. The nation currently ranks 43rd in
infant mortality rates among industrialized nations. In 2007, nearly seven of every 1,000 American babies died before their first birthday. The U.S. National Center for Health Statistics cited the high rate of premature births as the main reason for the nation’s poor ranking of infant mortality rates.

Even though many states improved their rates of premature birth, the March of Dimes still graded the United States with an overall C in its 2011 Premature Birth Report Card. The organization compared the nation’s 2009 rate of preterm birth (12.2 percent) with the March of Dimes’ new 2020 goal of 9.6 percent. In the most recent report card, only Vermont received an A grade. Sixteen states earned a B grade and 19 states, including Michigan, received a C. Eleven states and the District of Columbia received a D, while three states and Puerto Rico received an F.

In Michigan, the rate of babies born prematurely increased more than 10 percent between 1998 and 2008. One of every eight babies born in Michigan—295 in an average week — is born prematurely. And Michigan’s rate of preterm birth (12.7 percent) exceeds the national average of 12.2 percent. The state’s rate of premature birth actually increased from 12.5 percent, the rate recorded from 2005 to 2007.

The Michigan Department of Community Health reports that for every 1,000 live births in the state, eight infants die before their first birthday. Data compiled in 2009 by the Centers for Disease Control and Prevention and the Michigan Department of Community Health indicate Michigan’s infant mortality rate consistently exceeds the national average. In addition, there is an alarming disparity in the access to care, quality of care and pregnancy outcome among racial and ethnic groups in Michigan.

African-American mothers experience more birth complications, including more premature births, preeclampsia — a sudden and dangerous increase in blood pressure — and babies with low birth weight. Infants born to black mothers in Michigan are 70 percent more likely to be born prematurely than infants of other races, according to a 2010 report released by the Center for Healthcare Research & Transformation, a public policy and research organization based in Ann Arbor, Mich. Most babies are delivered between 38 and 40 weeks of gestation. However, 19 percent of babies born to black mothers in the state were born before 34 weeks of gestation, compared to 11 percent of white and Hispanic newborns. While the state’s rate of premature births held stable for births less than 34 weeks of gestation, the rate increased 20 percent among births between 24 and 27 weeks.

Premature births are costly. The Centers for Disease Control and Prevention report that preterm births topped the list of the most expensive hospitalizations in Michigan in 2007. Each premature birth in the state costs an average of $102,103 at the time of discharge from the hospital. That is 14 times the cost of a normal birth.

In his special message to the Legislature
in April 2011, in which he called for a new Michigan Office of Great Start - Early Childhood, Gov. Rick Snyder said that preparing children “for optimal learning and quality achievement in school actually begins at conception. Brain development begins early in a pregnancy. Threats, such as alcohol or malnutrition, can have a negative or even irreversible effect on the developing brain. Premature birth and low birth weight also can have lasting effects on a child. Early childhood is a time of remarkable brain growth that affects a child’s development and readiness for school.”

The office, Gov. Snyder said, will refocus the state’s early childhood investment, policy and administrative structures by assessing all public investments against a single set of early childhood outcomes, including children being born healthy.

Those who have dedicated their research lives to the Perinatology Research Branch at Wayne State University believe that pregnancy is where preventive medicine will begin in the 21st century. The team is led by Roberto Romero, M.D., D.Med.Sci., chief of the Perinatology Research Branch and one of the world’s leading experts in the study of complications of pregnancy. There is now evidence that many diseases such as cerebral palsy, obesity, diabetes, cardiovascular disease, high blood pressure and others begin to develop when the baby is in utero. Physicians and scientists at the branch are making great strides toward improving the diagnosis, treatment and prevention of pregnancy complications. A major focus of the team has been to identify the causes of premature birth.

The physicians and researchers of the Perinatology Research Branch have discovered that one of every four premature babies is born to a mother who has a “silent” intrauterine infection. Bacteria in the amniotic fluid induce an inflammatory response that leads to the onset of premature labor. The bacteria in the amniotic fluid can infect the fetus and cause multiple complications such as neonatal sepsis. The inflammatory response of the fetus may predispose to brain injury and cerebral palsy. These infections can involve the unborn baby and damage its brain when in utero.

Physicians and scientists working at the Perinatology Research Branch have developed rapid tests for the diagnosis of infection and identification of patients who may benefit from early antibiotic treatment, and have successfully treated such infections. They are finding ways to treat babies with the hope of preventing mental retardation and cerebral palsy. Some of these treatments involve the use of the latest medical science breakthroughs — such as nanotechnology — to deliver drugs directly to the affected organs.

The PRB team at Wayne State University has identified another major cause of preterm labor in which the mother’s immune system rejects the placenta and membranes. The placenta may be considered equivalent to a transplanted organ, because 50 percent of its genetic makeup belongs to the father. Normal pregnancy requires tolerance of this “transplanted” organ; however, if rejection occurs, there is malfunction of the placenta and membranes, which may lead to premature labor and delivery.

Research conducted at the branch continues to lead to discoveries that have translated into clinical advances in maternal-fetal medicine worldwide. The physicians and researchers of the branch have defined and characterized the fetal inflammatory response syndrome, which is responsible for birth defects such as cerebral palsy, as well as developed ultrasound algorithms for the diagnosis of congenital heart disease in babies. The branch also identified DNA variants that predispose
African-American women for premature delivery.

In 2011, one of those discoveries changed the way the world will treat pregnant mothers identified as at risk for premature birth. Studies conducted at the Perinatology Research Branch found that the rate of preterm delivery at less than 33 weeks can be reduced by nearly half simply by treating the mothers with a low-cost bioidentical form of natural progesterone gel from the mid-trimester of pregnancy until term. The study also showed that the use of vaginal progesterone reduced the rate of respiratory distress syndrome in newborns by 61 percent.

On behalf of the NIH, Dr. Romero was the principal investigator of the study. Sonia S. Hassan, M.D., the lead author of the study and WSU associate dean for Maternal, Perinatal and Child Health for the Wayne State University School of Medicine, noted that numerous studies — many conducted by the team at the Perinatology Research Branch — over the past decade have shown that ultrasound of the cervix can identify pregnant women who are at high risk for preterm delivery. The ultrasound is easy to perform, painless and can be performed between the 19th and 24th weeks of pregnancy. Pregnant women with a short cervix are at very high risk for preterm delivery. Once a high-risk mother has been identified, she can be offered treatment with progesterone.

“The findings of the study are especially good news for expectant mothers in Detroit,” said Dr. Hassan, professor of WSU Obstetrics and Gynecology. “Preterm delivery has long been a major health care problem in the city.”

In 2008, more than 17 percent of births in Detroit were preterm — and they accounted for more than 70 percent of the infant mortality recorded in that year, according to the latest research from the Michigan Chapter of the March of Dimes.

Another recent study conducted at the Perinatology Research Branch has taken a major step forward in determining the risk of a pregnant woman developing preeclampsia. The objective of the study was to determine whether concentrations of biomarkers measured in maternal blood in the first, second and third trimesters of pregnancy could predict the subsequent development of preeclampsia. The findings will help clinicians assess the risk for preeclampsia, and monitor mothers and their unborn babies at risk for the silent killer.

Estimates indicate that preeclampsia is responsible for 76,000 maternal deaths and more than 500,000 infant deaths every year, according to the Preeclampsia Foundation. Preeclampsia occurs only during pregnancy and sometimes after delivery. It is characterized by high blood pressure and the presence of protein in maternal urine. The unborn babies of preeclamptic mothers are affected by the condition and may develop intrauterine growth restriction or die in utero. Many experts believe preeclampsia results from insufficient blood supply to the uterus and placenta, causing the development of high blood pressure. The increase in maternal blood pressure is a compensatory response to improve the condition of the fetus. Preeclampsia may have evolved to protect the infant, but when the disease is out of control it threatens the health of the mother. The earlier the disease starts in pregnancy, the worse the outcome for baby and mother.

A related study conducted by the Perinatology Research Branch in women with preeclampsia received the prestigious Frederick P. Zuspan Award for Clinical Research from the International Society for the Study of Hypertension in Pregnancy. The award is given for the most outstanding clinical work relating to the study of hypertension in pregnancy.
The study found that maternal plasma concentrations of angiogenic and antiangiogenic factors, together with a combination of other demographic, biochemical and biophysical factors, are useful in assigning risk for the subsequent development of early-onset preeclampsia. The establishment of an accurate means to assess the risk for preeclampsia would enable health care practitioners to identify women who require more intensive monitoring to safeguard both mother and baby from this devastating condition. This study was the first of its kind in which women were prospectively followed from the beginning of pregnancy to determine if simple blood measurements can predict early onset preeclampsia. The results are very encouraging and suggest that the biomarkers studied can be used to identify women at risk in the second trimester, many weeks before the clinical onset of the disease.

The results of these studies will encourage laboratories and clinicians to use biomarkers to track the health of pregnant women. Several companies are developing methods to measure these biomarkers and hope to make them available for clinical use in hospitals throughout the world. These tests would allow health care practitioners to identify women at risk for preeclampsia.

A revolutionary discovery by the team of physicians and researchers led by Dr. Romero found that genetics plays a significant role in some preterm births and may explain why some women who do everything right still give birth too soon. The finding was recognized by the March of Dimes with its prestigious award for Best Research in Prematurity.

The study showed that genes of both the mother and the fetus can make them susceptible to an inflammatory response that increases the risk of a premature birth.

The team investigated the genes that control maternal and fetal inflammation that could help explain the process that triggers preterm birth. The research found that variations in the DNA of the pregnant woman and the fetus involved in fighting infection are associated with an increased risk of premature birth.

The central concept is that there are genetic factors that predispose to preterm labor and that are in the maternal and fetal genome. This was a step forward toward the idea of personalized medicine in the prevention of preterm birth.

Patients in the case-control study had at least one previous preterm birth. The researchers extracted DNA from the cord blood of 822 pregnant women and 807 fetuses, and then genotyped single nucleotide polymorphisms, or SNPs, in candidate genes that predispose to
preterm birth. A SNP involved in the control of fetal inflammation (IL6R) doubled the risk of preterm birth among the study subjects. DNA variants in maternal genes also increased the risk of preterm birth. Combined, these factors provide new evidence that a genetic predisposition to preterm birth can depend on the DNA of both mother and fetus.

Recognizing the significance of the breakthrough, the March of Dimes gave the study, “Identification of Fetal and Maternal Single Nucleotide Polymorphisms in Candidate Genes That Predispose to Spontaneous Preterm Labor with Intact Membranes,” its award for Best Research in Prematurity.

Researchers at WSU/PRB just this year demonstrated that a nanotechnology-based drug treatment in newborn rabbits with cerebral palsy enabled dramatic improvement of movement disorders and the inflammatory process of the brain that causes many cases of CP. The findings strongly suggest that there may be a window of opportunity immediately after birth for drug treatment that could prevent the condition.

The study is the first to show that an anti-inflammatory drug delivered with a nanodevice can dramatically improve CP symptoms in an animal model. The report, “Dendrimer-Based Postnatal Therapy for Neuroinflammation and Cerebral Palsy in a Rabbit Model,” was published April 18, 2012, in the prestigious journal Science Translational Medicine, published by the American Association for the Advancement of Science.

Cerebral palsy is a disorder of the developing brain that affects motor skills and muscle coordination, often not diagnosed until the age of 2 or 3 years in children. The United Cerebral Palsy Foundation, a national advocacy and support group, estimates that 764,000 children and adults in the United States have CP. According to the U.S. Centers for Disease Control and Prevention, 100,000 babies born in the U.S. develop CP annually. A 2009 report by the CDC indicated the prevalence of the condition at 3.3 per 1,000 births. Worldwide, the CDC estimates the prevalence of CP births to range from 1.5 to 4 for every 1,000 births.

The CDC estimates that the lifetime cost to care for a person with CP amounts to nearly $1 million (in 2003 dollars). The estimated combined lifetime cost for all Americans born with CP in 2000 is expected to total $11.5 billion in direct and indirect costs.

Risk factors for the condition include low birth weight and premature birth. Children born before the 32nd week of pregnancy are at high risk for developing CP. Intrauterine infection and/or inflammation is a major risk factor for CP.

Microglia — immune cells in the brain — play an important role in remodeling and growth during fetal and postnatal periods. Activation of these cells can cause an exaggerated inflammatory response, leading to brain injury and CP. Treatment is problematic because inflammation and the resulting injury can be spread throughout the brain’s white matter. Transporting drugs across the blood-brain barrier also represents a challenge.

The WSU/PRB team hypothesized that it was possible to deliver a drug using a tiny device (or nanodevice) that would cross the blood-brain barrier and target the activated cells (microglia and astrocytes) in the brain involved in neuroinflammation.

The researchers used a rabbit model of congenital CP because it replicates the type of neuroinflammation found in human brains and the resulting motor deficits observed in children with the condition. The method consisted of exposing fetal rabbits...
to endotoxin (a component of bacteria). Endotoxin induced inflammation of the fetal brain but did not induce the onset of labor. When the rabbits were born, they had great difficulties walking or hopping. The experiment consisted of treating affected rabbits intravenously with either a saline solution, a drug known as NAC (N-acetyl-L-cysteine) or a dendrimer coupled with NAC, also known as a D-NAC conjugate. Rabbits with CP treated with D-NAC on the first day of life showed a dramatic improvement and, within five days, were able to walk and hop. Rabbits treated with the NAC conjugate also showed a higher neuron count and lower evidence of inflammation compared to untreated animals.

N-acetyl-L-cysteine is an antioxidant and anti-inflammatory agent. It is being explored in several ongoing clinical trials to test its potential in autism spectrum disorders, pregnant women for the treatment of maternal and fetal inflammation, and Alzheimer’s disease. Dendrimers are synthetic biomimics of globular polymers of the amino acid alanine. Researchers are exploring their use as a vehicle to target drug delivery, a science known as nanotechnology.

The research team believes that conjugating NAC with dendrimers allows delivery of the drug directly to the cells involved, providing greater effectiveness. While still in preclinical testing in animals, the dendrimer-drug conjugate shows potential for postnatal treatment of babies suspected of having CP.

The therapy also holds promise for possible future treatments of neurological disorders, including multiple sclerosis. The brain, for the most part, can be divided into gray and white areas. Neurons are located in the gray area, and the white parts are where the neurons send their axons — similar to electrical cables carrying messages — to communicate with other neurons or muscles. Oligodendrocyte cells manufacture a cholesterol-rich membrane called myelin that coats the axons. The myelin’s function is to insulate the axons, much like the plastic coating on an electrical cable. In addition, the myelin speeds communication along axons and makes that communication much more reliable. Patients with multiple sclerosis display neuronal loss and myelin abnormalities that reduce the myelin coating.

The researchers found that D-NAC therapy also improved the production of myelin and reduced the neuroinflammation associated with the loss of myelin. In fact, by the fifth day after treatment with D-NAC, the CP rabbits demonstrated a significant increase in myelin that nearly matched healthy control animals.

“This is tremendous recognition of the research breakthroughs and the power of the partnership between Wayne State University, the Detroit Medical Center and the Perinatology Research Branch,” said Valerie M. Parisi, M.D., M.P.H., dean of the Wayne State University School of Medicine. “This study has the potential to pull back a curtain that has shrouded a medical challenge not just in relation to cerebral palsy, but with other conditions that affect millions around the world.”

The causes of preterm birth have long been shrouded in mysteries, and standard treatments aimed at stopping uterine contractions in women with premature labor have not been successful. Dr. Romero has previously proposed that preterm labor was not simply labor before its time, but the result of pathologic insults that trigger the onset of labor, and now the Perinatology Research Branch is unraveling those mysteries through the development of personalized maternal-fetal medicine.
Tinnakorn Chaiworapongs, M.D., of the Perinatology Research Branch and professor of the Wayne State University School of Medicine’s Department of Obstetrics and Gynecology, is the lead author of a study that has taken a major leap toward determining the risk of a pregnant woman developing preeclampsia.
While researchers have teased out many of the medical mysteries of pregnancy, preeclampsia remained a puzzle for decades. The condition, a sudden increase in blood pressure after the 20th week of pregnancy, is a leading cause of maternal and infant death worldwide. Those not killed by preeclampsia can suffer lifelong health problems.

Indicated by a sudden increase in blood pressure and protein in the urine, preeclampsia warning signs, in addition to elevated blood pressure, can include headaches, swelling in the face and hands, blurred vision, chest pain and shortness of breath. While the condition can manifest within just a few hours, some women report few or no symptoms at all. Physicians had no way of predicting which mothers would be hit with the condition.

Now, a study conducted by the National Institutes of Health Perinatology Research Branch at the Wayne State University School of Medicine has taken a major leap toward determining the risk of a pregnant woman developing preeclampsia. The findings will help clinicians around the world identify and monitor women who are at risk for developing the life-threatening condition.

Published in *The American Journal of Obstetrics and Gynecology*, the research set out to determine whether concentrations of biomarkers measured in maternal blood in the first, second and third trimesters of pregnancy could predict the subsequent development of preeclampsia. The findings of the study — the largest of its kind ever undertaken — will help clinicians assess the risk for preeclampsia and monitor mothers and their unborn babies at risk for the silent killer.

“Preeclampsia is one of the leading causes of maternal mortality. Despite several decades of research, the pathophysiology of this disease is not well known” said Tinnakorn Chaiworapongs, M.D., director of the Biomarker Discovery Unit of the Perinatology Research Branch and professor of the Wayne State University School of Medicine’s Department of Obstetrics and Gynecology. He served as lead author of the study, “A decrease in maternal plasma concentrations of sVEGFR-2 precedes the clinical diagnosis of preeclampsia.”

Estimates indicate that preeclampsia is responsible for 76,000 maternal deaths and more than 500,000 infant deaths every year, according to the Preeclampsia Foundation. Preeclampsia occurs only during pregnancy and sometimes after delivery. It can affect the liver, kidney and brain. Sometimes mothers develop seizures (eclampsia) and suffer intracranial hemorrhage, the main cause of death in those who develop the disorder. Some women develop blindness. The unborn babies of preeclamptic mothers are affected by the condition and may develop intrauterine growth restriction or die in utero.

Many experts believe preeclampsia results from insufficient blood supply to the uterus and placenta, causing the development of high blood pressure. The increase in maternal blood pressure is a compensatory response to improve the condition of the fetus. Preeclampsia may have evolved to protect the infant, but when the disease is out of control it threatens the health of the mother. The
earlier the disease starts in pregnancy, the worse the outcome for baby and mother. The biomarker test could prove especially important because women with preeclampsia often do not feel any effects until the condition is severe, at which point it becomes life threatening. Earlier detection is crucial to the health and life of the mother and her baby. The effects of preeclampsia on the mother include cardiac problems, possible brain hemorrhage, acute renal failure, blood clotting problems and possible blindness. If left undetected, the condition can progress to eclampsia and the mother may begin convulsing. For the fetus, preeclampsia has been connected to a reduction in placental blood flow, resulting in physical and mental disability, the slowing of fetal development, and in severe cases, infants may be stillborn.

According to the Preeclampsia Foundation, the condition, also known as toxemia or pregnancy-induced hypertension, affects five to eight percent of pregnancies. That means 6.6 million women worldwide were affected by preeclampsia in 2002.

Left untreated or undetected, preeclampsia can rapidly lead to eclampsia, one of the top five causes of maternal death and infant illness and death. Approximately 13 percent of all maternal deaths worldwide — the death of a mother every 12 minutes — have been attributed to eclampsia.

The foundation reports that preeclampsia is responsible for nearly 18 percent of all maternal deaths in the United States.

Even if treated successfully, preeclampsia can portend future health problems for mothers. Women who have had preeclampsia have double the risk for heart disease and stroke over the next five to 15 years after they are treated for the condition.

The Preeclampsia Foundation estimates that annually as a result of preeclampsia. The cost of the condition in the U.S., according to the foundation, is $7 billion annually, split between $3 billion a year in treating mothers and $4 billion a year for the cost of treating infants born prematurely because of preeclampsia.

The National Institutes of Health reports that while the proportion of pregnancies that involve gestational hypertension and eclampsia — the elevated level of preeclampsia — has remained constant in the United States over the last decade, the rate of preeclampsia has climbed by about 33 percent. The NIH points to an increase in the number of older mothers and multiple births as a partial cause for the higher numbers of preeclampsia.

The Perinatology Research Branch’s study received the Frederick P. Zuspan Award for Clinical Research from the International Society for the Study of Hypertension in Pregnancy. The award is given for the most outstanding clinical work relating to the study of hypertension in pregnancy.

“Our study found that maternal plasma concentrations of angiogenic and antiangiogenic factors, together with a combination of other demographic, biochemical and biophysical factors, are useful in assigning risk for the subsequent development of early-onset preeclampsia,” Dr. Chaiworapongsa said.

“The establishment of an accurate means to assess the risk for preeclampsia would enable health care practitioners to identify women who require more intensive monitoring to safeguard both mother and baby from this devastating condition,” said Valerie M. Parisi, M.D., M.P.H., M.B.A., dean of the School of Medicine. “This study is one the largest of its kind in which women were prospectively followed from the beginning of pregnancy to
determine if simple blood measurements can predict early onset preeclampsia. The results are very encouraging and suggest that the biomarkers studied can be used to identify women at risk in the second trimester, many weeks before the clinical onset of the disease.”

The results of the study will encourage laboratories and clinicians to use biomarkers to track the health of pregnant women. Several companies are developing rapid methods to measure these biomarkers and make them available for clinical use in hospitals throughout the world.

Dr. Chaiworapongs explained that these tests would allow health care practitioners to identify women at risk and to intensify monitoring. An important challenge still lies in finding methods to treat preeclampsia. He noted that defective angiogenesis may be observed in other complications of pregnancy such as premature labor, fetal death and intrauterine growth restriction. The markers are likely to identify not only patients with preeclampsia, but those at risk for other complications of pregnancy.

Research conducted in the labs of the Perinatology Research Branch has broadened the world’s understanding of perinatal medicine.
A revolutionary new discovery by a team of physicians and researchers led by the Perinatology Research Branch of the Eunice Kennedy Shriver National Institute of Child Health and Human Development/National Institutes of Health housed at the Wayne State University School of Medicine and Detroit Medical Center has found that genetics play a significant role in some preterm births and may explain why some women who do everything right still give birth too soon.

The research finding has been recognized by the March of Dimes with its prestigious award for Best Research in Prematurity.

The research, which was presented at the 30th annual Society for Maternal-Fetal Medicine meeting – “The Pregnancy Meeting” — in Chicago in 2010 and published in the American Journal of Obstetrics and Gynecology, demonstrated that the genes of both the mother and the fetus can make them susceptible to an inflammatory response that increases the risk of a premature birth.

Inflammation is a major risk factor for preterm birth. One out of every three premature births is associated with inflammation or infection. However, numerous studies have shown that treating bacterial infections in pregnant women does not prevent preterm labor.

A team of researchers at the Perinatology Research Branch and Wayne State University investigated genes that control maternal and fetal inflammation that could help explain the process that triggers preterm birth. The research found variations in the DNA of the pregnant woman and the fetus involved in fighting infection are associated with an increased risk of premature birth.

“The central concept is that there are genetic factors that predispose to preterm labor that are in the maternal and fetal genome,” said Sonia Hassan, M.D., associate dean for WSU Maternal, Perinatal and Child Health,
March of Dimes honors the PRB finding on genetic role in the mechanism of preterm birth with Best Research in Prematurity Award

A step closer to personalized medicine
by Phillip Van Hulle
and director of the Center for Advanced Obstetrical Care & Research within the Perinatology Research Branch. “We believe that this is a step forward toward the idea of personalized medicine in the prevention of preterm birth.”

Premature birth is a leading cause of infant death worldwide, with more than 500,000 such births in the United States. Premature birth is the most important risk factor for long-term disability, including cerebral palsy, chronic lung disease, blindness and deafness. The March of Dimes estimates that premature births in the United States alone result in an annual cost of $26 billion.

Patients in the case-control study had at least one previous preterm birth. The researchers extracted DNA from the cord blood of 822 pregnant women and 807 fetuses, and then genotyped single nucleotide polymorphisms in candidate genes that predispose to preterm birth. A SNP involved in the control of fetal inflammation (IL6R) doubled the risk of premature birth among the study subjects. DNA variants in maternal genes also increased the risk of preterm birth. Combined, these factors provide new evidence that genetic predisposition to preterm birth can depend on the DNA of both mother and fetus.

The next step in the research, Dr. Hassan said, is replication and sequencing of the IL-6 and IL-6 receptor gene.

Recognizing the significance of the breakthrough, the March of Dimes gave the study, “Identification of Fetal and Maternal Single Nucleotide Polymorphisms in Candidate Genes That Predispose to Spontaneous Preterm Labor with Intact Membranes,” its award for Best Research in Prematurity. Roberto Romero, M.D., D.Med. Sci., was the lead author on the study. This is the seventh study by Society for Maternal-Fetal Medicine members to receive the honor.

The March of Dimes is conducting a national Prematurity Campaign aimed at research and awareness to reduce the growing rate of premature birth.

“The March of Dimes is the organization that was determined to find a cure for polio and did so by supporting the development of the vaccine that is used now worldwide. Having accomplished this, the March of Dimes has identified the prevention of premature birth as a major health care problem in the world,” Dr. Hassan said. “We are honored for the recognition of the March of Dimes of the work done by the Perinatology Research Branch, Wayne State University, the Detroit Medical Center and its partners.”

“This research gives us even more evidence as to the relationship between genetics and preterm birth and is a step toward personalized medicine,” said Alan R. Fleischman, M.D., medical director of the March of Dimes. “This has the potential to allow us to identify a woman who is at risk for delivering early and provide her specialized, individualized care so that she may carry her baby to term, and help give more babies a healthy start in life.”

Other institutions collaborating in the research included the University of Miami, Emory University, Vanderbilt University, Genaissance Pharmaceuticals, and Sotero del Rio Hospital and Pontifica Universidad Catolica de Childe, in Santiago, Chile.
The Perinatology Research Branch (PRB) of the Eunice Kennedy Shriver National Institute of Child Health and Human Development housed at Wayne State University and the Detroit Medical Center is the nation’s nerve center of cutting-edge maternal-fetal medical research, but it also serves as a training ground for those who conduct such studies. The PRB offers highly sought-after fellowships to train physicians in providing specialized patient care in maternal-fetal medicine and prepare fellows for careers in academic medicine. The program seeks to develop tomorrow’s specialists in both clinical care and high-caliber medical researchers who will be responsible for the next wave of discoveries that will change the face of perinatal medicine.

To date, 53 physicians have completed fellowships in the Maternal-Fetal Medicine Fellowship program. Competition to be selected for a fellowship is intense. There are only seven doctors in the program at any one time. In 2011, 117 doctors applied to get into the program.

“We look for candidates who want to pursue a career in academic medicine,” said Sonia Hassan, M.D., associate dean for Maternal, Perinatal and Child Health and professor of Obstetrics and Gynecology for the Wayne State University School of Medicine. Dr. Hassan directs the Center for Advanced Obstetrical Care and Research, and oversees the Maternal-Fetal Medicine Fellowship, as well as the Combined Maternal-Fetal Medicine-Medical Genetics Fellowship. The
Wayne Medicine

fellowship is a combined program between the PRB, Wayne State University and the Detroit Medical Center and represents the only combined program of its kind. “After the three years, we hope that the fellows take away from the experience the desire to continue and perform research and make significant contributions to the field of maternal-fetal medicine.”

The three-year fellowships are specialty training. Those applying for the program are physicians who have already served a residency in obstetrics and gynecology.

In addition to immersion in clinical maternal-fetal medicine, each fellow conducts 18 months of intensive research related to the field. This way, the program develops physician-scientists who go on to improve direct patient care and to pioneer the way maternal-fetal medicine will be practiced in the future.

Zeynep Alpay Savasan, M.D., who originally is from Turkey, is in the final year of her maternal-fetal medicine fellowship. After receiving her medical degree from Istanbul University Medical School, she completed a Wayne State University-Detroit Medical Center residency in Obstetrics and Gynecology. During that time, she witnessed how WSU/PRB/DMC fellows were trained. She wanted similar training.

She had to apply and compete for one of seven positions. Her impressive record during her residency obviously helped her win one of the coveted positions. Dr. Savasan twice received the Outstanding Resident Award in Obstetrics and Gynecology/Maternal-Fetal Medicine, as well as the Best in Council of Resident Education in Obstetrics and Gynecology among first- and second-year Obstetrics and Gynecology residents at Wayne State University Award.

In the research portion of her fellowship, Dr. Savasan is focused on the immunologic aspects of obstetrical complications, including preterm labor, preterm prelabor rupture of membranes and intraamniotic infection/inflammation. Her research interests lie in reproductive immunology, the immunological basis of maternal-fetal tolerance and the pathophysiology of unexplained intrauterine fetal death.

“I am also studying the immunologic changes during term labor and term acute chorioamnionitis,” she said. “One of my other projects is the role of angiogenic/antiangiogenic factors in preterm labor, preterm prelabor rupture of membranes and intraamniotic infection/inflammation.”

While with the PRB, Dr. Savasan has published at least 15 maternal-fetal medicine research articles.

When she completes her fellowship, Dr. Savasan wants to pursue a career in academic medicine in the United States, where she can put into practice the clinical and research training she received at the PRB.

A native of Maracaibo, Venezuela, Eleazar Soto, M.D., received his medical degree from the Universidad del Zulia in his home country, and then completed a WSU-DMC residency.

Like his colleagues in the fellowship program, Dr. Soto stood out as a resident. He received the DMC Guild Research Award for Excellence, the Charles C. Vincent Award for Excellence in Obstetric Care, and was named Best Overall Resident in Obstetrics several times. He pursued the WSU/PRB/DMC fellowship to receive the best training possible, not only clinically, but academically.

“I knew that I could find this at the WSU/PRB/DMC. The years of experience and information generated in the field of maternal-fetal medicine and fetal ultrasound at the PRB attracted me to do this fellowship,”
Dr. Soto said. “Moreover, this fellowship has many world-renowned maternal-fetal medicine experts and has a multidisciplinary team that includes people working in basic science and ultrasound. The interaction with such a talented team was very appealing to me for my training.”

Now in his second year of fellowship training, he has published at least 27 research articles. His research interests lie in immunology of pregnancy and Great Obstetrical Syndromes, and fetal imaging.

He is exploring inflammatory markers in amniotic fluid and maternal blood of patients with a sonographic short cervix who are at risk of preterm delivery. Another area of study is the behavior of some angiogenic and antiangiogenic markers involved in the pathogenesis of preeclampsia.

“One of the most important things that I have learned from my fellowship, and that I am going to take with me, is the ability to critically evaluate the evidence that guides medical practice, including maternal-fetal medicine,” Dr. Soto said. “I have also learned that patient care, dedication, commitment, honesty and hard work are the keys for success in medicine.”

After completing his fellowship, Dr. Soto would like to enter an academic medical career while participating in the care of women with pregnancy complications “to obtain the best possible outcome for the mother and the future unborn child.”
Making a difference in Michigan

The State of Michigan is home to some of the foremost research institutions in the world. One shining example is the Perinatology Research Branch of the Eunice Kennedy Shriver National Institute of Child Health and Human Development/National Institutes of Health.

Since moving to Detroit in 2002, the Perinatology Research Branch has generated more than $300 million in economic impact, helped recruit world-class scientists to our state and treated nearly 20,000 at-risk pregnant women using breakthrough technology. Most importantly, the Perinatology Research Branch has been the epicenter of developing new research for the treatment of vulnerable Michigan mothers and babies.

One of the challenges with academic research is to translate scientific discoveries to the bedside of patients. Researchers at the Perinatology Research Branch at the Wayne State University School of Medicine have been working hard to change that.

The Perinatology Research Branch studied the effectiveness of progesterone in women with a shortened cervix, who have a significantly increased risk of giving birth prematurely. To our benefit, they recently released the results of this important study. The results are exciting as they have the potential to help reduce infant mortality in Michigan.

This is one example of how the Perinatology Research Branch is positively impacting our state. Of course, it has been an asset to Michigan since Wayne State University was awarded the Perinatology Research Branch in 2002.

Wayne State University now must compete for the next 10-year contract for the Perinatology Research Branch. While I believe the university’s track record should speak for itself, we should do all we can to help ensure the university is successful in this effort.

The Perinatology Research Branch and Wayne State University are strong partners and leaders in our crusade to reduce Michigan’s infant mortality rate. Their dedication to improving the health of Michiganders is commendable.

I look forward to our continued partnership. I am confident the Perinatology Research Branch and Wayne State University will continue to have a profound effect on the surrounding community and our entire state as we work to usher in a new era of health prosperity.

**Olga Dazzo**
Director
Michigan Department of Community Health
Research and economic incubator

National center of maternal-fetal medicine research helps fuel Michigan’s new economy

by Phillip Van Hulle
Michigan’s elected officials have rallied in support of having the Eunice Kennedy Shriver National Institute of Child Health and Human Development/National Institutes of Health maintain its Perinatology Research Branch at the Wayne State University School of Medicine, and it’s no wonder given that the branch is a maternal-fetal medicine research powerhouse and a much-needed medical facility for the state.

State Rep. Gail Haines introduced a resolution in the House Health Policy Committee on April 14, 2011, urging the Secretary of the U.S. Department of Health and Human Services keep the National Institutes of Health facility at Wayne State University once the current contract expires in 2012. Thirty more lawmakers co-sponsored the resolution, which the full House later adopted. The Michigan Senate Committee on Health Policy has adopted a similar resolution introduced by Sen. Jim Marleau.

A National Institutes of Health research center in maternal-fetal medicine, the PRB has been at the WSU School of Medicine, housed at the Detroit Medical Center’s Hutzel Hospital, since 2002 under a 10-year research grant. That contract is up for renewal in 2012, and Dean Valerie M. Parisi, M.D., M.P.H., M.B.A., said the School of Medicine will work hard to keep the branch in Detroit.

“The support from our elected officials is important and we value it highly,” Dean Parisi said. “The entire state and Midwest region need to realize the importance of keeping the PRB here. The branch is involved in crucial research that changes the way maternal-fetal medicine is conducted worldwide, and universities and health centers from across the country send their specialists here for training in cutting-edge medicine.”

Haines, who chairs the Health Policy Committee, said she introduced her bill because of her deep interest in medical research. “The Perinatology Research Branch is doing incredible work and will change medicine for years to come,” she said. “I commend Dr. Roberto Romero (chief of the PRB) and his team on the groundbreaking work they are doing. I look forward to continuing to support medical research statewide.”

She noted the branch’s “impressive list of research accomplishments, which were made possible because of the unique resources our region has provided to the facility. The PRB has been able to collaborate with the Wayne State University School of Medicine, which is regarded as one of the top urban health research centers and an institution with a high level of expertise in obstetrics and gynecological research."

The city of Detroit, in 2008, witnessed a premature birth rate of 17 percent, a rate that exceeds the national average of 12.5 percent. Those preterm births accounted for more than 70 percent of infant deaths that year, according to the Michigan Chapter of the March of Dimes. The city’s high infant mortality, preterm delivery rate and racial disparity in birth outcomes were key considerations in the NIH’s decision to locate the Perinatology Research Branch in Detroit.

The branch allows women to obtain state-of-the-art medical care and join medical studies to improve prenatal diagnosis, monitor fetal growth, predict preeclampsia and prevent preterm birth. To date, the branch has assisted more than 20,000 pregnant mothers.

Marleau, who chairs the Senate Committee on Health Policy, introduced his resolution
while noting the number of pregnant women — most from indigent households — who receive “world-class” care through the PRB and the WSU School of Medicine.

He also pointed out that Wayne State University and the Detroit Medical Center made significant investments in infrastructure to house the center. The state of Michigan and Wayne State University spent a combined $13 million to develop the offices and labs that house the branch and its staff.

“The work being done at Wayne State through the PRB program has made some of the most notable differences in the prevention of premature births in recent times and has done so amongst our most vulnerable residents,” Marleau said. “There is no question these achievements make this program an appreciating asset in Michigan's health care economy.”

The resolutions introduced by Haines and Marleau also recognized the “tremendous economic impact” the Perinatology Research Branch has in Michigan. The branch employs more than 130 physicians, researchers and staff members, many of them in high-paying technology positions the region needs as the state transitions to a new economic base. A study commissioned by the School of Medicine in 2010 estimated that the branch fueled an additional $35 million in economic activity in southeast Michigan.

In 2009, according to the report by Anderson Economic Group, the Perinatology Research Branch resulted in $8.7 million in salary and fringe benefits for employees. The average salary (including benefits) per employee totaled $65,530.

The state of Michigan receives an estimated $1.2 million in annual tax revenue as a result of the branch. Annual taxes paid to the city of Detroit amount to $176,000.

The cumulative economic activity associated with the branch during a second 10-year contract beginning in 2012, the Anderson Economic Group said, would exceed $347 million. New earnings going to Michigan residents over the life of a new contract would total $143 million.

Michigan’s congressional contingent also values the Perinatology Research Branch and the punch it provides Michigan in terms of a research powerhouse, benefactor of women and children, and stoker of the economy.

“I continue to support the effort to keep the NIH’s Perinatology Research Branch in Detroit,” said U.S. Sen. Carl Levin.

“Detroit is an ideal location for this important work, bringing together academic, research and clinical expertise, and the residents benefit greatly from the research done there.”

Referencing an announcement earlier this year that a study conducted at the PRB found that the daily use of a low-cost progesterone gel by mothers at risk for premature birth cut the level of preterm birth by as much as 45 percent, Levin said, “We celebrate the recent breakthrough and think it critical that this kind of work is allowed to continue undisturbed.”

U.S. Sen. Debbie Stabenow, who champions women’s health issues, said, “New medical discoveries at the Perinatology Research Branch at Wayne State University are saving the lives of babies and keeping mothers safe from serious pregnancy complications across...
With one in eight babies born prematurely in our state, this one-of-a-kind research center is making a real difference in the lives of Michigan families."

The PRB is situated in Michigan’s 13th congressional district. U.S. Rep. Hansen Clarke’s district is hit particularly hard by premature birth and its continuing health problems. He has toured the branch and met with its leaders.

“The Perinatology Research Branch at Wayne State University is leading the charge to advance the standards of perinatal care. Prenatal and perinatal care are two of the most important factors affecting both adult and infant health,” Clarke said. “Sadly, Detroit’s infant mortality rate is nearly 15 percent, placing Michigan in the top 15

states with the highest infant and neonatal mortality. Premature birth increases infants’ risk of future health problems and hospital care for these infants and mothers comprise some of the most expensive hospitalizations in Michigan.

“This center provides resources that enable our city to remain ground zero in the fight against infant/neonatal mortality and preterm births,” Clarke added.

“The PRB develops diagnostic, therapeutic and preventative maternal-prenatal strategies that improve pregnancy outcomes for our state and, ultimately, our nation. The PRB trains physicians and formulates best practices in order to advance the health care standards for pregnant women and their unborn children in underserved areas such as Detroit.”
Wayne Medicine recognized for state’s highest success rates

Burt and Gerley Weyhing, like millions of married couples, wanted to have children. The Grosse Pointe Farms couple, however, could not conceive — also like millions of married couples.

Today, though, they are the parents of twins Burt and Winifred, who were born May 29, 2010, “perfectly healthy and statistically average,” Burt Weyhing hastens to point out.

The couple also is quick to credit physicians of the Wayne State University Physician Group’s Division of Reproductive Endocrinology and Infertility for their eventual success in creating a family. That success was attained after two failed attempts with an infertility clinic in Florida.

“Emotionally and financially, it takes its toll,” Burt Weyhing said of the unsuccessful in vitro fertilization attempts. “But our first attempt with Wayne State University was successful and within three weeks we knew we were having twins. We knew that (twins) was something that could happen. We’re very excited to talk about this and very appreciative of their professionalism.”

The Weyhings — Burt, 43, and Gerley, 29 — are not alone. The U.S. Centers for Disease Control and Prevention reports that 7.3 million American women have used infertility services. The Michigan Department of Community Health, in a 2010 report, says that 10.2 percent of state adults age 50 and younger who were married or a member of an unmarried couple reported receiving some form of infertility treatment.
The CDC estimates that 11.8 percent of women between the ages of 15 and 44 have an impaired ability to have children. The number of married women in that age range deemed infertile — defined as the inability to become impregnated for at least 12 consecutive months — is 2.1 million, or 7.4 percent.

Like the Weyhings, many of these couples turn to in vitro fertilization to begin their families. The Weyhings eventually turned to the Wayne State University Physician Group’s Division of Reproductive Endocrinology and Infertility, which has the top pregnancy success rates for in vitro fertility in Michigan.

The division has the highest success rate of helping women 35 and younger achieve pregnancy and birth among infertility clinics in Michigan. The clinic’s success rate also exceeds the national average.

The clinic achieved a live birth rate among in vitro fertilization treatment with non-donor embryos of 65.2 percent for women 35 and younger in 2009, the most recent year for which numbers are reported. The national average success rate for clinics that year was 47.5 percent.

According to Fertility Success Rates (www.fertilitysuccessrates.com), the Wayne State University Physician Group clinic ranks 11th nationally in achieving live births through in vitro fertilization with non-donor embryos in patients 35 and younger. Fertility Success Rates based its rankings on data provided to the Society of Assisted Reproductive Technology, which tracks figures for infertility clinics across the nation.

The most recent SART information available shows the national success rate of births from non-donor fresh embryo transfers for women below the age of 35 is 47.5 percent.

“Patients come first. Everyone on our IVF team works beyond expectations to achieve these top IVF rates,” said Elizabeth Puscheck, M.D., M.S., Chair and professor of the Wayne State University School of Medicine’s Department of Obstetrics and Gynecology. “In this economy it is important to not only find the IVF clinic with the best pregnancy rates, but also one that offers financial support such as our ARC program provides. We are delighted to make IVF affordable to more people than ever before in Michigan.”

ARC, or Advanced Reproductive Care, is a national network of premier infertility programs that can provide affordable treatment packages and financing payment plan options for couples seeking to achieve pregnancy.

While Society of Assisted Reproductive Technology policy states that a comparison of individual clinic success rates may not be meaningful because patient medical characteristics, treatment approaches and entrance criteria may vary from clinic to clinic, the Wayne State University Physician Group Division of Reproductive Endocrinology and Infertility showed higher levels of success percentage-wise than the national average.

The division recorded a banner year for helping couples achieve pregnancy in 2009, said Dr. Puscheck and Manvinder Singh, M.D., associate professor of Obstetrics and Gynecology.
SART rates in 2010 showed the national success rate of births from non-donor fresh embryo transfers for women younger than 35 was 45.8 percent (38,372 attempts nationally). National pregnancy rates using thawed embryos for the same age range was 34 percent.

The Wayne State University clinic’s success rate for non-donor fresh embryo transfers in 2009 reached 78 percent. In the implantation of thawed embryos, the clinic achieved pregnancy rates of 54 percent in women younger than 35.

There are a number of reasons couples experience difficulties conceiving. Some women don’t ovulate or ovulate infrequently. They may be older, with a poor ovarian reserve — fewer viable eggs that may be more difficult to fertilize and implant, said Dr. Singh, the physician who helped the Weyhings conceive. Others have fallopian tubes blocked by infection, inflammation or endometriosis. Some women have previously undergone voluntary sterilization and now want to conceive again.

With many American women delaying pregnancy until they are in their 30s or 40s, age is a burgeoning factor in infertility rates, according to the CDC. Nearly 20 percent of women in the United States give birth to their first child after age 35, and one-third of couples in which the woman is older than 35 have trouble conceiving, the CDC said.

Many infertility statistics report numbers in terms of women, but difficulties in conceiving don’t always lie with women. A potential father may lack sufficient sperm for impregnation, have malformed sperm or sperm lacking sufficient motility. In other men, the path of sperm may be blocked because of a malformed vas deferens, the tubes through which sperm leave the testicles.

In the case of the Weyhings, Burt’s medical condition prevented the couple from conceiving naturally. The 43-year-old has hypogonadism, a condition marked by low testosterone that affects the production of sperm.

About 25 percent of couples seeking in vitro fertility assistance have multiple problems, Dr. Puscheck said. In initial evaluations, as many as 15 percent of couples don’t manifest an identifiable underlying cause that would prevent conception.

Dr. Puscheck said most couples who come to the clinic have been trying to conceive for a year or longer and are deeply frustrated by their inability to do so. “Several of our patients delayed child-bearing because they put career first. They are used to working hard to get what they want,” she said. “Unfortunately, biology is not like mathematics and there are not always answers.”

“By the time the couple comes to us they are ready to do anything to get a baby,” Dr. Singh said. “We’re pleased that we were able to help a high percentage of these patients start or complete their family. Seeing our patients’ reactions when they see and hear proof of their baby’s heartbeat for the first time is extraordinarily rewarding.”

The CDC estimates that 11.8 percent of women between the ages of 15 and 44 have an impaired ability to have children.

The CDC estimates that 11.8 percent of women between the ages of 15 and 44 have an impaired ability to have children.
Breathing easier

by Philip Van Hulle
Photos by David Dalton

Research duo uses education, coaching to reduce asthma morbidity and mortality in African-American teens

For many people, their only experience with asthma is laughing at the stereotypical nerdy kid sucking on his inhaler in movies or television sitcoms. Those who have asthma, or who have children suffering from the condition, aren’t laughing.

Asthma can be downright lethal, and in urban and minority populations such as Detroit’s, it’s a proven killer.

The rate of deaths from asthma for children in Detroit is 5.4 times higher than the rate for all Michigan children, according to the state Department of Community Health. The number of asthma-caused emergency room visits for children living in Detroit consistently tracks 60 percent higher than similar emergencies across the state. In 2006, the latest year for which statistics are available, the number of hospitalizations for asthma in Detroit outstripped statewide numbers, three to one.

Two Wayne State University School of Medicine researchers are using a National Institutes of Health grant to devise methods to decrease the frequency and severity of asthma attacks in minority children living in Detroit. Sylvie Naar-King, Ph.D., and Deborah Ellis, Ph.D., associate professors
Wayne Medicine

in the Department of Pediatrics and the Pediatric Prevention Research Center, secured a $2.4 million grant for their “Multisystemic Therapy to Reduce Health Disparities in Adolescents with Asthma” study.

Asthma, Dr. Naar-King said, is the most common cause of hospitalization for children, after infections. Minority children living in urban areas, especially adolescents, appear at risk for more frequent acute episodes and higher rates of death from the condition. “Poor illness management is thought to be a primary driver of asthma morbidity and mortality,” Dr. Naar-King said. “Yet, there are very few randomized, controlled trials with inner-city adolescents with asthma.”

The research conducted by Drs. Ellis and Naar-King matched recommendations by an Asthma Initiative of Michigan report, which states in part, “Michigan should develop projects aimed to understand the reasons for the dramatic racial and geographic disparities in asthma hospitalization rates.” The report also calls on the state to focus efforts to reduce the asthma “burden” in communities and populations with the highest asthma hospitalization rates. Specifically, AIM targets the city of Detroit for “immediate attention” in the form of public health efforts to improve asthma control and prevent “severe outcomes.” Established in 2000, AIM is a consortium of agencies that includes the MDCH, the American Lung Association, various health care centers and Wayne State University (among other universities). The goal is to collaborate and advance a statewide plan to combat and reduce Michigan’s asthma affliction.

Because of its complexity, Dr. Ellis explained, asthma management requires intensive, “multi-component” interventions to improve the lives of the children at highest risk.

Study investigators use Multisystemic Therapy to improve asthma management for high-risk African-American children ages 12 to 16 who have moderate to severe asthma. This should reduce emergency department visits and hospitalizations due to asthma attacks. Children who have been hospitalized at least once in the past year meet the high-risk qualification.

Multisystemic Therapy is an approach to disease management that consists of counselors visiting the homes of asthmatic children to advise families, with the help of experts, on how to modify the child’s environment, find a primary care physician and to assist with the development of medication schedules so that attacks can be limited in severity or avoided altogether.

Drs. Naar-King and Ellis have used Multisystemic Therapy previously in the treatment of teenage diabetic patients. That study, which consisted of six months of in-home therapy followed by 18 months of follow-up, showed that participating adolescent patients had significantly lower diabetic complications compared to a control group.

Standard asthma treatment protocol calls for at least two visits to a primary care physician annually. Medicaid data reveals that only 40 percent of Detroit children with persistent asthma had at least one such visit in 2004, making Detroit children covered by Medicaid the least protocol-compliant kids in the state.
If this protocol is not followed and prescriptions for corticosteroid inhalants — the primary first defense in the long-term control of asthma — are not filled, an attack can become acute, resulting in a costly trip to the emergency room. According to AIM, nearly 35,000 children in the state enrolled in Medicaid have persistent asthma, and that number is climbing. In predominantly African-American populations, rates of asthma emergency room visits are increasing as well. Only 70 percent of families with asthmatic children are filling prescriptions for long-term control medication. Only 55 percent of Detroit children with persistent asthma who are covered by Medicaid had a prescription for inhaled corticosteroid filled in 2004.

Clearly, the goals of asthma therapy are not being met for the urban pediatric population in Michigan, especially for African-American children, Dr. Naar-King said.

According to the state Department of Community Health and AIM, African-American children are hospitalized for asthma at a rate that is 4.2 times higher than that of white children. The prevalence of persistent asthma is 23 percent higher for African-American children than their white counterparts. African-American children visit emergency rooms for asthma at a rate 2.7 times that of white children, and children residing in urban counties are hospitalized for their asthma at a rate twice that of those from non-urban areas in Michigan.

AIM reports that the total cost of asthma in Michigan, according to the most recent calculations, is $394 million annually. If Multisystemic Therapy can lower the rate of emergency room visits, it could prove an effective means of reducing the costs of health care and hospitalizations.

The WSU study calls for a randomized, controlled trial with 170 adolescents. Eighty-five children will receive standard multidisciplinary specialty care and serve as a control group. The other 85 will receive standard care and Multisystemic Therapy. Families enrolled in the study will participate in an initial data collection session, a post-test after the completion of the seven-month program, and a post-test at 12 months.

“If successful, this intervention will provide immediate assistance to a vulnerable population disproportionately affected by asthma and may reduce costs of care for this high-risk population,” Dr. Naar-King said.
As soon as Angela Campau sat down to dinner, she began choking. Even though she had not yet picked up her fork, the choking began at the mere sight of food and the thought of swallowing it.

Campau was the victim of an incomplete brain signal, a sort of stuttering thought process akin to a scratched compact disc playing the same musical notes over and over. In this case, the music in her brain told the young girl that if she ate she would choke and die.

“I had choked so many times in public that my brain would tell my body that everything I tried to eat I would choke on,” Campau said. “When I was 10 I started to eat less and less, and then completely stopped eating. It caused me not to eat for close to two years, on and off.”

She subsisted on liquids like chicken broth, but even that presented difficulties in swallowing.

Her parents took Angela to a number of physicians seeking help. Some said it was a phase she would outgrow; others were at a loss for a diagnosis. Schoolmates teased her, claiming she was anorexic. “It made my life difficult, because in a way, I was depressed because I could not go along with my daily routine such as meals or going to people’s houses,” she said. “It was hard in school, especially at lunch, because all I really ate was chicken broth.”

When her parents brought Angela to David Rosenberg, M.D., the Miriam L. Hamburger Endowed Chair of Child Psychiatry and professor and interim Chair of Psychiatry and Behavioral Neurosciences at the Wayne State University School of Medicine, she was 11.

Dr. Rosenberg began treating her for obsessive compulsive disorder.

Campau, now 20 and fully in control of her OCD thanks to a combination of talk therapy and a prescription drug, said she finally feels “normal.”

“Now I live a normal life and eat everything I want. I can go out to dinner with family and friends and not have to worry about dying just from eating,” the Southgate resident said.

Obsessive Compulsive Disorder is a debilitating neuropsychiatric condition that affects approximately 1 percent to 3 percent of the population worldwide. According to the National Institutes of Mental Health, OCD affects about 2.2 million American adults. The disorder strikes men and women equally; as much as 80 percent of the time, symptoms are first detected in adolescence or early adulthood. Even though OCD is the fourth most common neuropsychiatric illness in the United States, the Obsessive Compulsive Foundation reports that less than 10 percent of OCD sufferers receive treatment.

A longstanding collaboration between researchers at different organizations led by Dr. Rosenberg discovered that children with OCD had abnormal glutamate levels in key brain regions, a situation that is reversible with effective treatment.

Along with Dr. Rosenberg, collaborators on the project included Frank P. MacMaster, Ph.D.; Yousha Mirza, M.D.; Phillip Easter, research assistant; and Michelle Rose, research assistant, of Wayne State University and Children’s Hospital of Michigan; Gregory Hanna, M.D., University of Michigan; Paul Daniel Arnold, M.D., Hospital of Sick Kids and the University of Toronto; and...
Margaret A. Richter, M.D., Tricia Sicard, research assistant, Eliza Burroughs, research assistant, and James Kennedy, M.D., of the University of Toronto. All brain images and blood samples were collected at Wayne State University with blood samples genetically analyzed in Dr. Kennedy’s and Dr. Arnold’s laboratory at the University of Toronto and Hospital for Sick Kids. The team published its findings in the March 2009 issue of the journal Brain Imaging and Behavior.

“Since our initial findings at Wayne State University, basic neuroscience, genetic, brain imaging and novel treatment development studies all converged to show that glutamate has a key role in OCD,” Dr. Rosenberg said. “If we think of serotonin as analogous to light that lets us see in the dark, glutamate is the brain’s light switch or brain modulator, which helps turn serotonin and other chemicals off and on.”

The studies found significant associations between glutamate receptor and transporter genes and abnormal brain volumes in brain regions implicated in OCD such as the thalamus (the “grand central station” of the brain), caudate nucleus (the brain’s “secretary”), anterior cingulate cortex (the
brain’s arousal center) and orbital prefrontal cortex (the brain’s “executive decision maker”).

Based in part on early findings at the School of Medicine showing glutamate abnormalities in OCD, new treatment approaches using glutamate modulator drugs such as riluzole, which is used for treating Lou Gehrig’s disease, have been used in adults and children with OCD. Studies using riluzole are being conducted by the National Institute of Mental Health in children with OCD. These clinical trials are not complete, so results are unavailable.

“This study at NIMH demonstrates how work first done at Wayne State University not only has scientific implications but has key translational relevance in bringing work from the bench to the bedside with potential clinical ramifications,” Dr. Rosenberg said. Wayne State University, the University of Michigan, the University of Toronto and the Hospital for Sick Kids in Toronto have submitted a collaborative R01 grant to the NIMH that is being considered for funding. Wayne State University is the lead site and coordinating center on this application.

The OCD research attracted the attention of Angela Campau, 18 in this photo, who was first diagnosed with OCD at age 11 by Dr. Rosenberg. Through a combination of talk therapy and a prescription drug, she says she now feels “normal.”
of ABC News producers at “Primetime,” and anchor David Muir interviewed Dr. Rosenberg and Campau for a segment on OCD.

“I agreed to do the interview because I knew how difficult it was for me, and I felt that I needed to help others with OCD by spreading my story,” Campau said. “I would tell others not to give up hope because there are people out there who can help you, and I would say what Dr. Rosenberg would say to me every time we met: ‘There is nothing bad in you that the good in you cannot fix.’”

A second paper published in the May 2009 issue of Psychiatry Research: Neuroimaging continued the team’s study of pediatric OCD patients and is the first published report examining the relationship between genetic variation and a neurochemical phenotype in OCD. This study found a significant association between variation in a key glutamate receptor gene and glutamate levels in the brain’s arousal center, the anterior cingulate cortex. No association was found between genetic markers and brain imaging measures in brain regions not implicated in the pathology of OCD.

“What we are doing is beginning to elevate child psychiatry to a level comparable to traditional pediatric medicine and neurology in that we now have a firm basis in the brain anatomy, chemistry and physiology, and, therefore, a better scientific underpinning for what we do, just like for other chronic medical illnesses like diabetes,” Dr. Rosenberg said. “The brain’s a lot more complicated in many ways, but the principles are the same. So we now know that childhood OCD is a brain disease and this knowledge may help defeat some of the stigma and prejudice children with psychiatric illness face, like more difficulty getting insurance to pay for their treatment or having people say, ‘It’s all in your head,’ when, in fact, these are brain illnesses that can be helped with proper treatment.

“Even the most imaginative science fiction writer could not have dreamed of the powerful tools we use routinely to look at the child’s brain,” he added. “With magnetic resonance imaging, we can take a completely noninvasive biopsy of the child’s brain anatomy, chemistry and physiology with great power and precision — but with no shots, needles or radiation. We take this brain biopsy without doing surgery.”
Turning the tide

by Philip Van Hulle and Julie O’Connor
Photos by David Dalton
WSU researchers set out to change high obesity rates among African-American children and teens

The people of the United States — and in particular Michigan — are fat and getting fatter, making it more and more difficult to gird our collective, more corpulent loins, for the battle against obesity.

The rise in rates of obesity in adults — and in our children — has itself spawned an epidemic of attempts by government units to police our food intake: New York City banned the use of trans-fats by restaurants. Soft drink and vending machines are being removed from public schools or restocked with more nutritious items. Laws have been adopted mandating that fast-food restaurants must post nutritional values and the caloric content of the items on their menus.

While obesity is a growing problem for all Americans, it poses a greater problem for African-Americans, particularly in children and adolescents. There haven’t been many studies of interventions designed to prevent or treat obesity among this population, and those attempted have largely failed. However, a team of researchers at Wayne State University have set out to address this problem with the support of a five-year, $5.7 million grant from the National Heart, Lung and Blood Institute and the Eunice Kennedy Shriver National Institute of Child Health and Human Development, both of the National Institutes of Health.

The obesity center is headed by Sylvie Naar-King, Ph.D., associate professor of Pediatrics in the WSU School of Medicine, and K-L Catherine Jen, Ph.D., professor and Chair of Nutrition and Food Science in WSU’s College of Liberal Arts and Sciences. Collaborators from the Medical University of South Carolina as well as nine departments and institutes at Wayne State University are involved in the project.

“What we are doing is specifying what needs to happen to actually learn and use skills,” said Dr. Naar-King. “By increasing intrinsic and extrinsic motivation through various methods, participants will develop and practice skills in the context in which they occur. An example is having a community health worker present at meal times to help the family measure food portions.”

Dr. Naar-King, also a member of the School of Medicine’s Pediatric Prevention Research Center, explained that the intervention project consists of three components: strategies to increase extrinsic motivation, strategies to increase intrinsic motivation and skills development. Primary skills of parental monitoring of adolescent eating and exercise will be a key, as will self-monitoring of food intake and exercising, managing hunger and cravings, and portion control.

According to the 2009 “Overweight and Obesity in Michigan” report produced by the Michigan Department of Community Health, nearly 29 percent of high school students in the state were either overweight or obese based on body mass index measurements taken in 2007. And it’s not just the kids — the same report showed that obesity in Michigan adults climbed 21.8 percent between 2001 and 2008 to a point where nearly 70 percent of adults in Michigan were considered overweight or obese. Among adults, blacks had a 39.8 percent obesity rate,
while 28.8 percent of whites were obese. Slightly more than 42 percent of black women in the state were obese, the highest rate of any race/gender group. In all, Michigan’s 30.1 percent was the eighth highest obesity rate in the United States. After the Sanilac area (39.1 percent), Detroit had the highest prevalence of obesity at 38.1 percent.

In 2000, the U.S. Centers for Disease Control and Prevention put the nation’s cost of obesity-related health care at $117 billion. By 2008, that amount rose to $147 billion. Between 1987 and 2001, obesity-related diseases in the nation accounted for 27 percent of the increase in all medical costs. The center estimated that the cost of medical expenditures for obese workers was 29 percent to 117 percent higher than comparable costs for workers of normal weight. In real dollars, this translates into $3,785 to $38,270 more for those who are obese, according to the Ann Arbor-based Center for Healthcare Research & Transformation.

In the 2007-2008 National Health and Nutrition Examination Survey, the CDC found that 17 percent of children and adolescents ages 2 to 19 were obese. In the 20-year period ending in 2008, the obesity rate in pre-school children jumped from 5 percent to 10.4 percent and the rate in elementary school students increased from 6.5 percent to 10.6 percent. Among teens between the ages of 12 and 19, obesity increased from 5 percent to 18.1 percent. Interestingly, 84 percent of parents believed their children were at a “healthy” weight, despite these findings.

“Overweight and obese youth are at increased risk for heart disease, diabetes, stroke, osteoarthritis and several types of cancer,” said Dr. Jen, whose research focuses on the area of induced obesity and diabetes, as well as maternal and infant nutrition. “They are also at risk for significant psychological and social adjustment problems, such as poor self-esteem. In addition to these serious consequences of overweight and obesity, these health outcomes also place a significant burden on the health care system.”

CDC researchers blame the obesity epidemic on a combination of societal issues. Some Americans, particularly those in urban areas, have less access to markets selling fruit and vegetables. Six of every 10 adults drink at least one sugary drink, such as soft drinks, daily. It is easier and less expensive in most areas to purchase less healthy or fast food. The CDC also points to heavy advertising for foods high in fat, sugar and salt.

We also have a tendency to drive everywhere rather than walk and are more sedentary than our ancestors. Few students now get time for quality physical education during the school day. The 2005 Michigan Youth Risk Behavior Survey showed that 33 percent of ninth-through 12th-graders did not engage in the recommended amount of weekly physical activity. Thirty-six percent of that age group spent three or more hours of every school day watching television. Only 38 percent attended a physical education class on one or more days during the school week due to at least a decade of budget cuts forcing school districts to trim classes that are not considered essential for basic education.

Studies indicate that obesity-related diseases such as Type 2 diabetes, elevated cholesterol, cardiovascular disease and kidney failure occur at higher rates in obese children just as they do in obese adults. And because obese children are very likely to become obese adults, the diseases are present for much longer in the life cycle, making symptoms in adults more acute.

In their report, “F as in Fat: How Obesity Threatens America’s Future 2010,” the Trust for America’s Health and the Robert Wood
Johnson Foundation point out that 19 states have set nutritional standards for school meals that are more strict than current United States Department of Agriculture requirements. Twenty-seven states have nutritional standards for other foods sold at school, such as items sold in vending machines, school stores or at bake sales. Twenty states have adopted requirements for BMI screenings or other weight-related assessments of students. In Michigan, a new round of nutritional guidelines for schools has been launched that, in addition to promoting healthier eating in cafeterias, attempts to de-emphasize food for celebrations like birthdays in elementary classrooms.

The Michigan Department of Community Health reports that in 2005, almost one in four Michigan adults purchased meals from a fast-food restaurant two or more times per week. The prevalence of fast-food consumption in blacks was higher (30.4 percent) than whites (23.9 percent). The rates of obesity increased in accordance with the number of weekly visits to fast-food eateries, from 24 percent for less than one visit per week to 32.9 percent for more than three per week. The chances of a Michigander being obese were nearly 60 percent greater for those

Sylvie Naar-King, Ph.D., and K-L Catherine Jen, Ph.D., lead a five-year study to identify successful weight-loss intervention strategies among obese African-American children. Once identified, the methods can be adopted throughout communities in North America.
eating fast food two or more times weekly, according to the 2009 “Overweight and Obesity in Michigan Surveillance Report.” In 1958, about 5 percent of meals and snacks were purchased from fast-food restaurants. In 2007, that number jumped to 37 percent. MDCH says that in 2008, 78.3 percent of state adults ate an inadequate amount of fruit and vegetables. It was worse for children — 83 percent consumed inadequate amounts of fruit and vegetables, and nearly 30 percent drank at least one non-diet soda or soft drink daily. The lack of sufficient fresh fruit and vegetables is a real problem in urban Detroit, which some have described as a “food desert.”

“A study released in 2010 by researchers from Yale University reports that 84 percent of parents said their children had eaten fast food in the past week. Members of the Rudd Center for Food Policy and Obesity at Yale said preschoolers see at least three television commercials per day from the likes of McDonald’s, KFC and Taco Bell. Teens see five a day.

While we are consuming greater amounts of food, we are eating less nutritiously. The lack of sufficient fresh fruit and vegetables is a real problem in urban Detroit, which some have described as a “food desert.”

“One of the many initiatives to improve health in the city of Detroit involves increasing resources for fresh produce,” Dr. Jen said. “We anticipate that the community health workers will help the family identify feasible options to access fresh produce and problem-solve to increase the use of these options by the families. We plan to stay

Families enrolled in the multi-component, home-based behavioral weight-loss program will be taught how to monitor their food intake and make healthier meal choices.
involved with and aware of produce programs and locations so that we can share them with the families.”

Those same children and teens who did not eat enough fruit and vegetables also did not reach the basic vigorous or moderate physical activity goals set by the Healthy People 2010 initiative. Black children and teens recorded the highest prevalence of excessive television viewing and computer or video game use, according to the MDCH.

The WSU project will guide adolescents and their families through various sets of treatment options. Through these phases, the participants will learn and practice skills that will help them adhere to weight-loss strategies through healthier eating options and improved exercise programs. They will be taught to trim about 500 calories from their daily food intake and how to monitor physical activity levels. “The goal is to identify the most effective interventions to motivate African-American teenagers to adhere to weight-loss strategies,” Dr. Jen said. “Community health workers will be trained to use home-based or community-based intervention to maximize behavioral changes in these teenagers.”

So far, counselors and researchers have found they need a variety of carrots, rather than sticks, to keep families on track with proper eating and exercising skills. Some families respond better to skills training with motivational conversations, Dr. Jen said, while others need prize-based incentives. “When it comes to obesity prevention and treatment, it is not one-size-fits-all,” Dr. Jen said. “Hence, it is important to provide options to adolescents in order to identify the optimal strategy.”

Families for the study were recruited through the Adolescent Medicine Clinic, the General Pediatrics Clinic and the Health and Fitness Clinic at Children’s Hospital of Michigan, as well as at school health clinics, community centers and health fairs. In all, about 260 families will be enrolled in the study.

The adolescents involved are at or above the 95th percentile of body mass index for their age. The body mass index scale is a measure of body fat based on height and weight that many health experts have adopted to supplant old insurance company height and weight charts. In a 10-year-old boy, a BMI of 18 would indicate a healthy weight, while 21 would be overweight. A score of 23 would be classified as obese. In adults, “normal” weight falls between 18.5 and 24.9 on the BMI scale, while “overweight” runs between 25 and 29.9, and “obese” is 30 and higher. The children in the study average 240 pounds and a BMI of 39.7.

Dr. Naar-King said the research team members will streamline the vast amounts of weight management information while community health workers support the development of internal and external motivation in the families on a personal level. The families are required to make committed steps to overcome environmental and societal cues that lead to weight gain. The program allows families that may otherwise not have access to structured weight-loss programs the chance to receive the support they need to succeed.

Over the five years of the study, the research team expects to develop insights into the “what” families need in order to develop and maintain healthy dietary and exercise behaviors as well as what community health workers need in terms of training and support to maximize sustained positive outcomes.

“Community involvement is a key component to success, and we also hope to build area partnerships as a foundation for larger, community-based participatory programs,” Dr. Jen said.
Deans, Chairs and Directors

Vice Deans

Robert A. Frank, M.D.
Clinical Affairs

Kenneth P. Lee, CPA
Business Affairs

Maryjean Schenk, M.D., M.P.H., M.S.
Education

Roberta Sonnino, M.D.
Faculty Affairs

Bonita Stanton, M.D.
Research

Associate Deans

Gerold Bepler, M.D., Ph.D.
Cancer Programs

Patrick Bridge, Ph.D.
Undergraduate Medical Education

Scott A. Gruber, M.D., Ph.D.
Veterans Administration Affairs

Sonia Hassan, M.D.
Maternal, Perinatal and Child Health

Henry Lim, M.D.
Henry Ford

Tsveti Markova, M.D., F.A.A.F.P.
Graduate Medical Education

Silas Norman Jr., M.D.
Admissions, Diversity & Inclusion

Robert Pauley, Ph.D.
Graduate Programs

Daniel A. Walz, Ph.D.
Research

Assistant Deans

Matthew Jackson, Ph.D.
Basic Science Education

Lisa MacLean, M.D.
Student Affairs and Career Development

Renee Page, M.D.
Clinical Sciences

David Pieper, Ph.D.
Continuing Medical Education

Herbert C. Smitherman Jr., M.D., M.P.H.
Community and Urban Health
Department Chairs

Douglas Bacon, M.D., M.A.  
Anesthesiology

Gerold Bepler, M.D., Ph.D.  
Oncology

John Boltri, M.D., F.A.A.F.P.  
Family Medicine & Public Health Sciences

Michael L. Cher, M.D.  
Urology

John M. Flack, M.D., M.P.H.  
Internal Medicine

Murali Guthikonda, M.D.  
Neurosurgery

Linda D. Hazlett, Ph.D.  
Anatomy & Cell Biology

Lawrence Horn, M.D.  
Physical Medicine & Rehabilitation DMC

Jian-Ping Jin, M.D., Ph.D.  
Physiology

Mark Juzych, M.D.  
Ophthalmology

Omar Khan, M.D.  
Neurology

Andre Konski, M.D., M.B.A., M.A., F.A.C.R.  
Radiation Oncology

Robert H. Mathog, M.D.  
Otolaryngology

Darius R. Mehregan, M.D.  
Dermatology

Jay M. Meythaler, M.D., J.D.  
Physical Medicine & Rehabilitation  
Oakwood

Bharati Mitra, Ph.D.  
Biochemistry & Molecular Biology

Paul Montgomery, Ph.D.  
Immunology & Microbiology

Lawrence Morawka, M.D.  
Orthopaedic Surgery

Brian O’Neil, M.D.  
Emergency Medicine

Elizabeth Puscheck, M.D., M.S., F.A.C.O.G., C.C.D.  
Obstetrics & Gynecology

David Rosenberg, M.D.  
Psychiatry & Behavioral Neurosciences

Wael A. Sakr, M.D.  
Pathology

Ashok Sarnaik, M.D., F.C.C.M., F.C.C.P., F.A.A.P.  
Pediatrics

Bonnie F. Sloane, Ph.D.  
Pharmacology

Wilbur L. Smith Jr., M.D.  
Radiology

Donald Weaver, M.D.  
Surgery

Center and Institute Directors

Lawrence I. Grossman, Ph.D.  
Center for Molecular Medicine & Genetics

Karin Przyklenk, Ph.D.  
Cardiovascular Research Institute
Wayne State in 30 seconds

Wayne State combines the academic excellence of a premier research university with constructive, hands-on experience in an urban environment that is a microcosm of the real world. Excellence and experience prepare WSU graduates to excel immediately.