Taking the Complications Out Of Pregnancy: Groundbreaking Discoveries by the Perinatology Research Branch Leading to Healthier Pregnancies and Lives

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Taking the complications out of pregnancy

Groundbreaking discoveries by the Perinatology Research Branch leading to healthier pregnancies and lives

The Perinatology Research Branch of the Eunice Kennedy Shriver National Institute of Child Health & Human Development of the National Institutes of Health, located at Wayne State University and Hutzel Hospital, is leading studies on complications of pregnancy. The research team led by Roberto Romero, M.D., chief of the Perinatology Research Branch (PRB), has made seminal discoveries in the disorders responsible for premature birth, birth defects and infant mortality in the United States.

Preterm birth affects 12% of pregnancies and costs $26 billion annually in the United States alone. Moreover, premature babies are at increased risk for short- and long-term complications such as cerebral palsy and developmental disorders. The causes of preterm birth have been a mystery, and the standard treatments aimed at stopping uterine contractions in women with premature labor have not been successful. Romero proposed that preterm labor was not simply “labor before its time,” but the result of pathologic insults that trigger the onset of labor.

The work of the PRB and WSU has identified that one of every three preterm babies is born to a mother who has a “silent” infection in the amniotic cavity. Bacteria in the amniotic fluid induce an inflammatory response that leads to the onset of premature labor. Sometimes, the bacteria in the amniotic fluid infects the fetus and can cause multiple complications such as neonatal sepsis, and the inflammatory response of the fetus may predispose to brain injury and cerebral palsy. Physicians and scientists working with Romero have developed rapid tests for the diagnosis of infection and those patients who may benefit from early antibiotic treatment.

Preterm birth occurs more frequently when the mothers have relatives who had delivered a premature baby; also, women who were born premature themselves are at higher risk of delivering a premature baby. This suggests that genetic factors may alter the risk for preterm delivery. Romero’s team has recently identified specific DNA variants in mothers and fetuses that increase the risk of premature labor/delivery. Of interest is that many of the DNA variants that predispose to prematurity were located in genes that control the inflammatory response in mother and baby. This research recently received an award from the March of Dimes for the “Best Research in Prematurity.”

This research at the PRB provides support for the introduction of personalized medicine during pregnancy. Such personalized medicine would be unique in that it must take into account the genetic makeup of the mother and the fetus - until now, personalized medicine focused solely on one patient.

Recently, the PRB identified another major cause of preterm labor in which the mother’s immune system rejects the placenta and membranes. The placenta is considered equivalent to a transplanted organ because 50% of its genetic makeup belongs to the father. Normal pregnancy requires tolerance of this transplanted organ, however, if rejection occurs, there is a malfunction of the placenta and membranes which may lead to premature labor and delivery. Romero and his team have discovered a molecular signature for rejection in amniotic fluid and are now working on methods to treat such rejection.

The latest groundbreaking clinical study led by the PRB of a new method for preventing premature birth in millions of women each year, was published in the medical journal *Ultrasound in Obstetrics & Gynecology*. The study, “Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial,” showed that the rate of early preterm delivery in women (<33 weeks) can be reduced by 45 percent simply by treating pregnant women who have a short cervix with a low-cost gel of natural progesterone during the second trimester of pregnancy until term.

“The study offers hope to women, families and children,” said Romero. “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.”

Romero, principal investigator of the study, and Sonia S. Hassan, M.D., professor of obstetrics and gynecology in WSU’s School of Medicine, director of the WSU/PRB/DMC Maternal-Fetal Medicine Fellowship Program and lead author of the study, also pointed out that numerous studies (many by the PRB) over the past decade have shown that ultrasound of the uterine cervix can identify...
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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 (<20mm) are at very high risk for preterm delivery.

Romero added that once a mother at high risk for preterm delivery has been identified, she can be offered treatment with progesterone. Of major interest is that progesterone reduced the risk of preterm delivery not only at <33 weeks, but also at <28 weeks (one of the secondary endpoints of the study). It also reduced the rate of respiratory distress syndrome, the most common complication of premature babies.

“We believe that the data in our study speaks for itself – and we predict that it will have major implications for obstetrics.”

“The findings of the study are especially good news for expectant mothers in Detroit,” said Hassan. “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.

The city’s high infant mortality rate, preterm delivery rate and ethnic disparity in birth outcomes were important considerations in the NIH’s decision to establish the PRB in Detroit nine years ago. The presence of the PRB in Detroit 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.

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

Describing the startling results, which showed that the rate of preterm birth among the women with a short cervix had been reduced by 45 percent, Hassan noted, “The main implication for clinical practice is that universal screening of women with ultrasound examination in the midtrimester to identify patients at risk (based on a short cervix) can now be coupled with an intervention – the administration of vaginal progesterone gel – to reduce the frequency of preterm birth and improve neonatal outcome. This can be accomplished conveniently.”

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

Our group has been working on this approach to reducing infant mortality for much of the past decade, and it’s very exciting to see that the effort is paying off, and that mothers and infants will soon be able to benefit from it.”

These findings are an example of research that is quickly translated into improved clinical care outcomes. The pioneering contributions of the PRB will be shared around the world to benefit pregnant women and unborn children so that they can lead healthier and happier lives.

About Dr. Roberto Romero: Dr. Romero received his undergraduate degree from San Vincente de Paul and his medical degree, magna cum laude, from the University del Zulia, both in Maracaibo, in Venezuela. He has been chief of the Perinatology Research Branch of the National Institute of Child Health and Human Development of the National Institutes of Health since 1992.

About Dr. Sonia Hassan: Dr. Hassan received a B.A. in psychology and communications with distinction from the University of Michigan, and an M.D. from Wayne State University. She joined Wayne State University in 2001 and has been with the Perinatology Research Branch since 2006.

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