'Science' features advances in preterm birth

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The Aug. 15 edition of the journal *Science* features a major article about the most important problem in obstetrics: preterm labor. The article, "Preterm labor: one syndrome, many causes," delivers a powerful message: preterm birth is not one condition, but many, and provides a framework for meeting this challenge.

"There are 15 million preterm babies born annually, and the condition affects 5 percent to 15 percent of all pregnancies, with the highest rates in North America and Africa. Prematurity is the leading cause of infant death up to age 1and the second-leading cause of childhood death before the age of 5," said Roberto Romero, M.D., D.Med.Sci., chief of the Perinatology Research Branch of the Eunice Kennedy Shriver National Institute of Child Health and Human Development located at Wayne State University and the Detroit Medical Center. "We have made

progress by identifying the causes of premature labor, and now we propose that it is possible to reframe the problem and make it tractable."

A common belief is that preterm labor is merely labor that starts too soon. This perception derives from the fact that labor, whether term or preterm, has the same features – increased uterine contractility, opening of the cervix and rupture of the membranes. "However," Dr. Romero said, "the fundamental difference is that normal labor at term occurs when the uterus and placenta cannot continue to support the growth of the fetus within the womb. In contrast, preterm labor results from several disease states."

Dr. Romero considers premature labor a syndrome – a collection of syndromes and signs – caused by multiple disease processes. A typical example of these disease processes is a "silent" intra-amniotic infection. Bacteria normally present in the vagina sometimes ascend into the amniotic cavity, triggering inflammation that in turn initiates premature labor.

From an evolutionary perspective, Dr. Romero explained, the onset of premature labor in the context of infection can be considered to have survival value, because it allows the mother to expel infected tissue (the membranes and fluid) and maintain reproductive fitness for a future pregnancy. This unique mechanism of maternal host defense comes at a price: prematurity.

Physicians and scientists at the PRB are now asking why some women develop a "silent" infection that can cause preterm labor and rupture of membranes, and some do not.

Other patients do not have infection, but have other disease states. For example, some women present with vaginal bleeding and uterine contractions, and they have inadequate blood supply to the placenta.

Studies at the PRB, WSU and DMC show that some patients with premature labor have very narrow spiral arteries, which fail to expand and do not provide sufficient blood supply to the placenta. Researchers are investigating biomarkers in maternal blood that can identify these patients.

Another fascinating discovery is that maternal anti-fetal rejection can explain some cases of premature labor. The fetus and placenta express both maternal and paternal antigens, and are therefore allografts (or transplants). The placenta has been considered the most successful transplant in nature. However, sometimes the mother rejects the paternal antigens expressed in the placenta, and this causes preterm labor. New research taking place at WSU, DMC and the PRB is focused on the identification of biomarkers responsible for maternal anti-fetal rejection.

Premature labor can also begin by a decline in progesterone action. Progesterone is essential for the maintenance of pregnancy and keeps the cervix closed until the onset of labor at term. A decline in progesterone action leads to a short cervix, which predisposes to premature labor. The administration of vaginal progesterone to patients with a short cervix can reduce the rate of preterm birth by 45 percent, as well as the rate of respiratory distress syndrome, the most common complication in premature babies. A policy of universal cervical screening is being implemented in Detroit, coupled with the administration of vaginal progesterone.

"Progress in the prevention of premature labor will require deciphering the mechanisms of disease, the identification of specific biomarkers and implementation of therapeutic interventions," Dr. Romero said. "The PRB, Wayne State University and the Detroit Medical Center have created a unique partnership to study the biome of pregnancy and how it is altered in premature labor. This promising initiative will support a new

knowledge-based economy in Detroit."

Dr. Romero recognized the exceptional vision of WSU President M. Roy Wilson, the University's Board of Governors, WSU School of Medicine Dean Valerie M. Parisi, M.D., M.P.H., M.B.A.; the leadership of the DMC; and the city of Detroit for "making possible many of the discoveries described on the pages of *Science*, for much of this work has taken place in Detroit."

Provided by Wayne State University