

Advances in Research: Screening Test

Blood pressure cuffs, urine dipsticks, and the scale: for decades, these simple tools have aided health care providers in the detection of preeclampsia. As a woman's pregnancy progresses, her prenatal visits come closer together, so that her weight gain, urine, and blood pressure readings can be monitored for signs of the disorder. However, this system isn't perfect. While preeclampsia most frequently occurs at term, it can sometimes strike much earlier. The disorder can sometimes progress rapidly between appointments, or the warning signs can be too subtle to trigger alarm.

But soon, clinicians may have another method for detecting preeclampsia: a reliable screening test that can spot changes in the bloodstream relatively early in pregnancy, warning healthcare providers when preeclampsia may occur before term.



In the past eight years, a substantial amount of preeclampsia research has focused on proteins found in blood known as soluble factors. The chain of events that will eventually lead to preeclampsia seems to begin quite early in pregnancy -- in fact, during the implantation of the placenta. Something disrupts the implantation process. As pregnancy progresses, the placenta intermittently runs short of oxygen, and the levels of many of these soluble factors start to vary from normal.

One of these proteins raises maternal blood pressure and inhibits Placental Growth Factor, or PlGF. Another protein, called soluble endoglin (sEng), also affects blood vessel function and is particularly elevated in HELLP syndrome. The hope is that by measuring levels of PlGF and sEng, the ratio between them, and the rate at which they are changing, clinicians can detect preeclampsia much sooner, well before symptoms appear. At that point, monitoring and management of that pregnancy would become more aggressive, in expectation that she will develop the symptoms of the disease as pregnancy continues.

Several companies in the United States and abroad have invested in these and other biomarkers to develop diagnostic or screening tests.

Miraculins Inc., a company that develops diagnostic tests from academic research and further adapts them for clinical use, first acquired the rights to an ensemble of 35 soluble factors, including endoglin, from Mount Sinai hospital. On January 7, they announced a new partnership with Inverness Medical Innovations Inc., a company that manufactures and markets such tests worldwide. "It was just a natural fit for us," said Ferran Prat, Vice President of Oncology and

Women's Health for Inverness. "We're [already] launching a PlGF test in Europe, where the regulatory environment is different."



Christopher Moreau, President and CEO of Miraculins, plans to launch the first US ELIZA-based test through a few labs within the year, under a FDA exemption called an ASR, to build data while progressing towards full FDA approval. One way to apply the test would be to take a blood draw around the 24th week of pregnancy and compare it with first trimester bloodwork. This could detect changes that warn that a woman is likely to develop early preeclampsia, before 35 weeks gestation. The test could likely also be used as an instant diagnostic confirmation that a woman less than 35 weeks pregnant is suffering from preeclampsia and needs immediate treatment. The test itself only requires basic infrastructure and when the costs of the phlebotomist and shipping, if needed, are factored in, the total price will likely be \$100- \$200.

Preliminary serum and plasma studies indicate that the test will have very high sensitivity and specificity, which means it will capture essentially all of the women who will go on to develop early preeclampsia, plus a small number of women who will be monitored more closely but won't go on to develop the disease before 35 weeks gestation.

And there's hope for a first trimester screening test within a few years. "We're delighted to be able to move forward with developing this test," said Moreau. "Maternal and child health has been terribly neglected, and the opportunity to do something positive for women in this position, and save lives, is just tremendous."