

Novel lab test may advance diagnosis of rare but dangerous pregnancy condition

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A laboratory blood test developed at Johns Hopkins for the diagnosis of a rare genetic red blood cell disorder also shows promise in identifying HELLP syndrome, a life-threatening high blood pressure condition affecting 1 percent of all pregnant women that causes hypertension along with end organ damage, researchers report in the May issue of the journal *Experimental Hematology*.

The findings, based on a study of [blood](#) samples from a small number of [women](#), suggests that the two conditions have similar underlying biochemistries marked by over activation of a part of the immune system called the alternative pathway of complement. If confirmed in further and larger studies, the test, a modified form of an assay for broken [red blood cells](#) known as a Ham test, could be used to identify women who could benefit from medicines to block increased complement activation, according to senior study author Robert Brodsky, M.D., director of the Division of Hematology at the Johns Hopkins University School of Medicine.

"The clinical implications from an obstetric point of view are potentially huge," says lead study author Arthur "Jason" Vaught, M.D., a maternal fetal medicine fellow at Johns Hopkins. "If this works, we can reduce pre-term deliveries, stays in the neonatal [intensive care unit](#) and other complications for mothers and their babies."

Brodsky was part of a team that developed the modified Ham test that measures levels of components of serum, , a protein-rich liquid in blood,

and showed it was effective in diagnosing atypical hemolytic-uremic syndrome (aHUS), a genetic disorder in which abnormal blood clots form in small blood vessels in the kidneys. That work was published in 2015 in the journal *Blood*.

Because aHUS and HELLP syndrome share similar traits—such as hemolysis, or the breakdown of red blood cells; elevated liver enzymes; a low platelet count; kidney dysfunction; [high blood pressure](#); seizures; and altered mental status - the investigators thought the test also could be used to identify HELLP syndrome.

HELLP is thought to be a severe form of preeclampsia, a pregnancy complication marked by high blood pressure and potential kidney and other organ damage, says Vaught; preeclampsia occurs in 3 to 5 percent of all pregnancies. The acronym stands for a syndrome composed of hemolysis, elevated liver enzymes and low platelet count. Currently, there is no diagnostic blood or biomarker test, and the condition is diagnosed only by the appearance of its symptoms.

The only treatment for HELLP, whose origins are not well understood, is delivery of the infant. Because HELLP can occur any time after the 23rd week of pregnancy, babies delivered to address the disorder are generally premature, and must spend time in a hospital [neonatal intensive care](#) unit, Vaught says.

In the current study, investigators used the modified Ham test to study serum samples from 14 women with classic or atypical HELLP syndrome, seven women with severe preeclampsia, 11 women with normal pregnancies, and eight healthy non-pregnant women. All pregnant women were at least 23 weeks pregnant.

The authors found increased complement activation, as measured by the modified Ham test, in women with classic or atypical HELLP, compared

to those with normal pregnancies or those not pregnant. Researchers observed average cell killing of 34.3 percent in those with classic HELLP, and 26 percent in atypical HELLP compared to an average 5 percent in those with normal pregnancies and 3.3 percent in those who were not pregnant.

Next, in a laboratory test-tube experiment they found that mixing serum from women with classic or atypical HELLP together with a monoclonal antibody that blocks complement, resulted in a significant decrease in the killing of cells in the modified Ham test—from about a 34% kill rate down to a 5% kill rate, the amount seen in healthy individuals.

The results add to evidence that HELLP is associated with increased complement activation, and that its origins relate to aHUS, Brodsky says. While this may not explain 100 percent of cases, "it probably explains the majority of them and gives us a pathway, complement, to target for potentially treating HELLP syndrome."

More information: Arthur J. Vaught et al, Direct evidence of complement activation in HELLP syndrome: A link to atypical hemolytic uremic syndrome, *Experimental Hematology* (2016). [DOI: 10.1016/j.exphem.2016.01.005](https://doi.org/10.1016/j.exphem.2016.01.005)

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