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From Diagnosis to Delivery: A Look at the Continuing Gap in Maternal Testing

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Guest: Dr. Ann Gronowski is a professor in the Department of Pathology & Immunology at the Washington University School of Medicine in St. Louis, MO.

Bob Barrett: This is a podcast from *Clinical Chemistry*, a production of the Association for Diagnostics & Laboratory Medicine. I'm Bob Barrett. Globally, the pregnancy-related mortality rate has decreased dramatically in the last 100 years, thanks largely to advances in medicines such as sterile technique, antibiotics, and blood transfusions.

Despite this improvement, mortality rates remain disproportionately high in lower- to middle-income countries, and the World Health Organization [WHO] has set a goal to reduce maternal mortality to half of what it is today by the year 2030. Surprisingly, in 2017, the WHO reported that the United States was one of only two countries to show a significant increase in maternal mortality.

In addition, the maternal death rate for Black pregnant women in the U.S. is 2.5 times the rate for White pregnant women. Diagnostics can play a crucial role in improving pregnancy-related outcomes by enabling early detection and management of complications. Yet, a significant gap remains in the diagnostic tools available for pregnant patients. The January 2026 issue of *Clinical Chemistry* published a special report that provides a look at the continuing gap between what is needed to improve maternal care and what is actually available.

One of the authors, Dr. Ann Gronowski, is here with us today to discuss this topic. Ann Gronowski is a professor in the Department of Pathology & Immunology at the Washington University School of Medicine, and her research focuses primarily on the laboratory diagnostics of endocrinology and reproductive physiology, with a particular emphasis on maternal-fetal medicine. Dr. Gronowski, let's start with the basics here. Why did you feel it was important to write this special report, and what did you hope to accomplish?

Ann Gronowski: Yeah, so recently the March of Dimes came out with a report that said that the United States again earned a D-plus grade for the fourth consecutive year for preterm birth. The national preterm birth rate remains at 10.4 percent. I think that most people, even healthcare professionals, don't realize

that the United States has such a poor maternal mortality rate.

Of course, the reason for this is multifactorial, but as you mentioned, laboratory testing could play an important role in improving outcomes. However, lab testing can help only if we have tests with excellent clinical utility and we have proper interventions. So as a laboratorian, I think it's important for us to critically evaluate the testing that is available, outline the limitations, and define what's needed, and that's what this paper hoped to accomplish.

Bob Barrett: So, what are the primary causes of maternal morbidity and mortality?

Ann Gronowski: The primary causes of maternal death remain infection, hemorrhage, cardiovascular events, and hypertensive disorders. Pregnancy-related morbidities include short- and long-term health problems that arise from pregnancy or childbirth itself and include hypertension, gestational diabetes, anemia, and miscarriage. In the United States, the pregnancy-related morbidity and mortality may be increasing because of the high rates of obesity, diabetes, and chronic hypertension.

Bob Barrett: And why is it so difficult to develop laboratory tests for use during pregnancy?

Ann Gronowski: Yeah, that's a great question. So first of all, to develop predictive tools, we need large prospective patient cohorts. However, for relatively low-prevalence diseases like ectopic pregnancy or preeclampsia and preterm delivery, thousands of patients need to be recruited, preferably before exhibiting symptoms, in order to include enough affected patients.

Second is that pregnancy is a moving target. Concentrations of many blood components change dramatically during pregnancy, thereby requiring serial collection through gestation and storage of tens of thousands of samples. And finally, women's health historically has been understudied for various reasons, including lack of funding, fear of harming unborn fetuses, and the reluctancy of pregnant patients to enroll in studies.

Bob Barrett: Dr. Gronowski, your paper presents five examples of pregnancy-related conditions for which you feel a significant diagnostic gap still exists. So, why not put them all in a hat, pull one out, and explain some of the gaps you see?

Ann Gronowski: Sure. Let's pick preeclampsia. This is a serious hypertensive disorder that occurs alongside with organ damage, most commonly the kidneys. There are a variety of risk factors associated with the development of preeclampsia, including

multifetal gestations, renal disease, preeclampsia in a previous pregnancy, and gestational diabetes.

But most cases occur in first-time mothers with no obvious risk factors, making it difficult to study. Focus has been placed on the ratio of serum concentrations of something called soluble FMS-like tyrosine kinase 1, or sFlt, and PlGF, or placental growth factor. This test has been FDA-approved. This ratio is increased prior to the development of preeclampsia and has an excellent negative predictive value, indicating patients that will not develop the disease.

But the pretest probability of developing disease in a low-prevalence population is, by its nature, very low. So, a test with a high negative predictive value really provides little more than a flip of a coin. So, a test with a high positive predictive value is really what's needed.

In addition, the only treatment for preeclampsia is delivery. So, we lack a good test and a good treatment. So, I personally believe that sFlt/PlGF ratio is not ready for standard of care use, but it could be useful in identifying patients who should be enrolled in studies that examine new treatments for preeclampsia.

Bob Barrett: Well, finally, Dr. Gronowski, looking ahead, what is needed to improve maternal and fetal morbidity and mortality?

Ann Gronowski: Well, this is a multifactorial problem that will require multiple solutions. For the three conditions that lead to the majority of maternal fetal morbidity and mortality, including preterm delivery, preeclampsia, and ectopic pregnancy, affordable, effective, and rapid modes of testing are needed. But that won't be enough without safer, more effective treatments.

One of the complexities is that these are low-prevalence conditions with potentially catastrophic outcomes. And for this reason, a single test needs extremely high sensitivity and specificity in order to achieve the necessary positive predictive value. Alternatively, we can take a two-step approach with a highly sensitive screening test to accurately identify high-risk pregnant women, followed by a highly specific or diagnostic test to identify who to treat.

Another problem is lack of access to high-quality testing. Just for example, given the superiority of non-invasive prenatal testing, maternal serum screening really should be discontinued entirely. It's difficult for me to understand how all pregnant women are not given access to cell-free DNA testing. But, of course, cost is the barrier. Likewise, cell-free DNA testing can be used to determine the RhD status of a fetus, which helps prevent hemolytic disease of the newborn in subsequent pregnancies.

So, by analyzing maternal plasma for fetal DNA, the Rh status of the fetus can be determined even before the mother has been sensitized. And this information allows for targeted administration of Rh immune globulin only when necessary, potentially conserving resources and reducing the risk of unnecessary Rh immunoglobulin administration. Cell-free fetal DNA for Rh status has been adopted widely in countries outside the United States, but in the United States, the anti-natal administration of Rh immune globulin to RhD-negative patients is the standard of care for reducing the risk of alloimmunization. So, as you can see, it's complicated, and there's no single easy solution.

Bob Barrett: That was Dr. Ann Gronowski from the Washington University School of Medicine in St. Louis, Missouri. She wrote a special report in January 2026 issue of *Clinical Chemistry*, describing the ongoing unmet needs in maternal testing, and she's been our guest in this podcast on that topic. I'm Bob Barrett. Thanks for listening.