Letters

AMH immunoassays

October 2018—In the article “Satisfaction high with new automated AMH assays” (June 2018), the focus seems to be on the presumed advantages of the Roche Elecsys and Beckman Coulter Access automated anti-müllerian hormone assays over manual AMH assays. The article reports that the main advantages of the automated platforms are less variability in AMH measurements, greater assay turnaround time, and greater assay cost-effectiveness. These are easily quantifiable metrics, and they beg to be quantified in the article. Assay sensitivity, specificity, and accuracy are not well addressed or supported by peer-reviewed data.

The opening comments about follicle-stimulating hormone as a marker are conflicting because they imply there are a lot of data to support its use, but then describe it as a late marker of lost reserve and a poor predictor of outcome without explaining why this is important or how AMH measurements address this apparent deficiency.

A reproductive endocrinologist says in the article that the lack of an international standard for AMH is a problem. While an international standard is valuable for assay methods to demonstrate traceability, this is not the problem that has led to a manufacturer’s lot-to-lot variation, nor is it the cause of the differences between the two automated AMH systems. The reproducibility of a method from lot to lot, instrument to instrument, and lab to lab is not related to the implementation of an international reference standard.

A laboratory manager posits that sample preparation and transportation stability were causes of preanalytical variability and that samples had to be shipped frozen and protected from light. There is no evidence to support a claim that AMH concentration in a serum or plasma sample is light sensitive. The laboratory manager said they sent 50 test specimens to another laboratory that would also use the Roche AMH automated assay and the comparison met the “requirement for AMH to be validated . . . without the need for retesting,” but she did not explain their acceptance criteria. In-house testing and validation and verification involved two labs testing against one another using the same instrument. While this is acceptable for a proficiency testing program, it is not appropriate assay validation because they could both have the wrong answer.

The frozen sample studies are poorly described. We are told that AMH was stable and that the laboratory ran samples at -20° and +20° and “couldn’t break it.” Surely what was meant is that samples were stored at -20°C and at room temperature (approximately 20°C) and then assayed for AMH. However, the number of freeze-thaw cycles and the length of time in storage at those temperatures are not provided, nor is it explained how the four percent difference from the supposedly fresh specimen was calculated. In contrast to what another laboratory manager reports in the article, this laboratory’s conclusion is that AMH is stable. In fact, AMH is a stable analyte; specimen collection, preparation, and storage/transportation are not different from most protein hormones. The reader is led to believe, however, that an automated AMH assay conveys sample stability that did not exist before. The analyte instability claims were perpetuated mainly in an attempt to shift blame from a poorly controlled assay.

It is often assumed, as it was in your article, that manually performed assays are more error- and variance-prone than an automated assay. The main source of AMH variability in the older tests was not operator error, as suggested. The concerns with the older assays were well researched and debated, but unfortunately they were not adequately published.[1]

We agree that AMH is not likely to be a marker of pregnancy success in non-fertile women, but it still has utility in determining reproductive health relative to ovarian reserve and menopausal status so that women can plan when to start a family. The follicle pool will be in decline over time with age until menopause. AMH is reflective of that follicle pool, and its accurate measurement is meaningful in understanding a woman’s reproductive function and health throughout her natural reproductive life, whether or not she is trying to conceive. AMH is a valuable tool to identify women with a diminished ovarian reserve. In PCOS (polycystic ovary syndrome), high serum AMH correlates strongly with a high antral follicle count. Early diagnoses or reproductive function disorders can help

physicians intervene and possibly prevent or ameliorate comorbidities of diminished ovarian reserve and PCOS throughout women's reproductive lives and after menopause.

1. Clark CA, Laskin CA, Cadesky K. Anti-Mullerian hormone: reality check. *Hum Reprod.* 2014;29(1):184–185.

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