Tests used in the diagnostic evaluation of infertility: from ubiquitous to obsolete

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The only true wisdom is in knowing you know nothing.

-Socrates

In the June 1967 issue of *Fertility and Sterility* Drs. Robert Glass and Adnan Mroueh published, "The post coital test and semen analysis," where they analyzed 112 semen analysis and post coital tests (PCT) over the course of one year (1). They noted a robust correlation between a normal semen analysis and normal PCT. They however failed to demonstrate any correlation between an abnormal PCT and semen analysis parameters. This was one of many papers that ultimately led to the demise of the post coital test as part of the routine infertility evaluation.

As we look back over the past 50 years, there have been a number of tests that were once considered routine that are no longer performed by most reproductive medicine specialists. The zona-free hamster oocyte penetration assay was developed in the early 1980s. This test used heterologous insemination of human sperm with zona-free hamster eggs. Early observations suggested that only acrosome reacted sperm were capable of fusing with the eggs. Yang et al. (2) later published a study showing that sperm from fertile donors and infertile patients with normal or abnormal semen analyses displayed similar capacity to undergo the acrosome reaction in vitro. As a result, most abandoned this test.

In the 1990s there was excitement that antibodies directed against sperm surface antigens (antisperm Ab) might exert a fertility-reducing effect. Antisperm Ab have been found in semen as well as serum from the female partner. These antibodies were blamed for negatively impacting spontaneous conception via sperm cell agglutination and also preventing migration into cervical mucous. The presence of antibodies in the semen was also thought to inhibit proper attachment of sperm to the oocyte and thereby inhibit fertilization. Antibodies found in the female serum were hypothesized to negatively impact ART outcomes by reducing fertilization and pregnancy rates. A well designed study by Hershlag et al. (3) failed to show a negative impact on the presence of anti-sperm antibodies in the arena of ART and this test was also forsaken.

In the late 1990s and early 2000s, the endometrial biopsy was routinely performed in the luteal phase as part of the infertility evaluation. Tissue was examined to see whether it was "in phase" or "out of phase" and it was widely accepted that "out of phase" was inconsistent with implantation. In 2004, a large multi-center prospective study by the Reproductive Medicine Network (4) demonstrated that out of phase biopsy results poorly discriminated between women from fertile and infertile couples and again another test was deemed obsolete.

The advancement in our understanding of human reproduction has led to astounding progression in the diagnostic and treatment modalities for infertility. While right now it seems suppositious that today's tests will become antiquated, one must wonder what the writers of this column in 50 years will classify as such.

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