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COMMENTARY

The question of sperm DNA fragmentation testing in the male infertility work-up: a response to Professor Lewis' commentary

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Abstract A response to the Commentary 'Should sperm DNA fragmentation testing be included in the male infertility work-up?' by Professor Sheena Lewis.

KEYWORDS: DNA integrity, in-vitro fertilization, intracytoplasmic sperm injection, intrauterine insemination, male infertility, semen analysis

Professor Lewis (Lewis, 2015) makes some strong arguments and raises some important questions about routine testing of men for DNA fragmentation (DNA-F) during a work-up for infertility. It is indeed disappointing that data are inadequate to recommend routine DNA-F testing.

Sperm DNA-F has not consistently been shown to distinguish between couples who will or will not become pregnant with expectant management, intrauterine insemination (IUI), IVF or IVF–intracytoplasmic sperm injection (ICSI). In a large number of studies, men who achieved fertilization, pregnancy or live birth were shown to have lower sperm DNA-F than men who did not. These studies, however, also show that some couples with high sperm DNA-F are able to become pregnant using less invasive and less costly methods within a time frame that is reasonable for many couples. Other studies have failed to find a difference in outcome for men that differ in sperm DNA-F. A lack of consensus still remains on the utility of these tests.

Although DNA-F testing is promising as part of male infertility diagnosis, we do not have sufficient evidence of its predictive value to recommend universal adoption of this methodology, largely owing to the small, heterogeneous populations, variations in methodology and inadequate experimental designs of existing studies (Zini, 2014). If studies are underpowered, have defects in design and are heterogeneous, it is not evidence-based medicine to recommend application of the results to the entire patient population. The editorial (Drobnis and Johnson, 2015) did not suggest that the European Society of Human Reproduction and Embryology (ESHRE) position report (Barratt et al., 2010) opposed DNA-F testing; rather that the ESHRE report, along with the American Society for reproductive Medicine Practice Committee guidelines (ASRM Practice Committee, 2013), recommend that more research is needed. The widespread use of ICSI before its safety was evaluated in experimental species is not a shining moment in reproductive medicine (de Wert, 1998); indeed, clinical trials in humans, before animal experiments, violates the Nuremberg Code and the Declaration of Helsinki. We are very fortunate that ICSI did not have adverse outcomes analogous to those with Thalidomide several decades earlier.

Even with its problems of accuracy and precision, semen analysis has an important place in diagnosis of male factor

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infertility; it is inexpensive and can suggest treatment or further testing of the infertile man. It is exactly the determination of a man's fertility by natural conception that is relevant when beginning the work-up of an infertile couple. In general, a man producing two or more abnormal semen analyses, at an appropriate interval, should be evaluated by a practitioner trained in male infertility (ASRM Practice Committee, 2015). An abnormal seman analysis can be a symptom of life-threatening conditions, some emergent, including extreme high blood pressure, testicular cancer and brain tumour (Esteves et al., 2011; Jarow, 1994; Jequier, 2006). The man should receive evaluation and treatment for his infertility before considering medical interventions to achieve a pregnancy. Because it adds independent information to the semen analysis, DNA-F testing is likely to be helpful in determining the best treatment, if healthy lifestyle changes or medical therapy do not allow the patient to achieve a pregnancy on his own. It should be remembered, however, that this testing is expensive and, in most of the world, the cost is borne by the patient.

The possibility that ICSI improves pregnancy outcome over IVF alone in cases with high DNA-F, is exciting, and Professor Lewis' theories on the mechanisms for this are intriguing. High pregnancy and live birth outcomes are achieved by ICSI. If the goal in treating infertile couples were to achieve a pregnancy as rapidly as possible, then all patients, should begin by using IVF–ICSI. However, assisted reproducutive techniques are costly, invasive, potentially involve adverse outcomes, and are generally reserved for cases for which other treatment have a low chance of success (ASRM Practice Committee, 2012; Carrell et al., 2015). Sperm DNA-F testing may be the test we need to identify couples requiring assisted reproductive techniques, donor insemination or adoption.

In addition to information gained by the fertility work-up of the man and woman, other social and financial concerns may affect the couple's decision on which fertility treatment is best for them. An important consideration for worldwide reproductive health is that assisted reproductive technique treatments are inaccessible for many infertile couples. In the USA, medical insurance does not cover assisted reproductive techniques in most states, and one cycle of IVF costs about 20% of the median household income (US$52,000 per year in 2013). Worldwide, many infertile couples currently benefit from the less expensive and less invasive treatment of intrauterine insemination, even though the per-cycle pregnancy rate is relatively low, and not all patients will achieve success (Ombelet et al., 2014).

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