Editorial

Despite limitations, sperm DNA fragmentation testing provides unique information complementary to but distinct from semen analysis results

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Drs. Tadros and Sabanegh highlighted three critical aspects regarding the clinical utility of sperm DNA fragmentation (SDF) testing in their commentary (1) concerning the recently published practice recommendations for SDF testing based on clinical scenarios by Agarwal *et al.* (2). First, the authors noted that SDF testing faces similar shortcomings as of conventional semen analysis as regards its ability to discriminate couples who will or will not become pregnant naturally or by ART. Second, Drs. Tadros and Sabanegh pointed out that similar to semen analysis, SDF tests lack standardization. And lastly, they pondered that SDF testing adds cost to the infertility workup as it is not covered by insurance companies.

Foremost among all is perhaps the ability of SDF testing to predict pregnancy. Since SDF test results are not binomial, that is, 'yes' or 'no', and pregnancy is an endpoint widely influenced by female factors, it seems unlikely that any SDF assay will be able to provide highly accurate discriminatory information (3-5). As shown by the Longitudinal Investigation of Fertility and the Environment (LIFE) study, SDF was negatively associated with time to pregnancy (TTP), but several other factors influenced TTP, including sperm morphology, and both male and female age (6). TTP, calculated as the time taken from stopping contraception to achieving pregnancy, provides an estimate of the per cycle probability of conceiving a clinically detectable pregnancy (7). In the LIFE study, which enrolled approximately 500 couples in the United States with no infertility history discontinuing contraception for the purpose of becoming pregnant, SDF was associated with fecundability (6). Like other predictive factors mentioned above, SDF should not be used in isolation. However, if taken in conjunction with other parameters, SDF results may provide unique information complementary to but distinct from semen analysis results (8-10).

Second, although it has been commonplace to criticize SDF testing on the grounds of a lack of standardization, as noted by Tadros and Sabanegh, a genuine effort has been made to overcome this situation. For instance, both SCSA and SCD assays have been standardized (11-13), and the manufacturer of the Halo test® provides easy-to-follow information on how to implement and conduct SDF analyses in andrology laboratories (14). Along the same lines, the TUNEL assay using a benchtop flow cytometer has been recently standardized and validated (15-16). In this sense, the time has come for incorporation of SDF to the andrology armamentarium provided robust methodology is followed.

Lastly, it is true that SDF testing adds cost that is usually paid by couples. However, the cost of testing should be weighed in the face of the potential benefits on an individual basis. For instance, it might be worth to offer SDF testing to couples before embarking on ICSI as some evidence indicates that in face of high SDF—the use of testicular sperm (Testi-ICSI) is advantageous over ejaculated sperm (17). In one study, the number

of couples needed to treat to obtain an additional live birth by Testi-ICSI was about five, which means 1 out of 5 cycles of ovarian stimulation and ovum pick-up could be avoided (17).

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Footnote

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