Commentary

Sperm DNA integrity testing: a valuable addition to the tool box of infertility clinicians

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ART (assisted reproductive technologies) clinicians worldwide should take note of the recent article by Agarwal *et al*. (1), which provides both a pertinent and timely recommendation; the combined evaluation of oocyte quality and sperm DNA integrity represents a critical step towards achieving reproductive success, whether via natural conception or following ART.

In recent years, a large consensus has formed, confirming the fact that gamete quality is a major determinant of reproductive success. In the case of the sperm, the fact that sufficient numbers of spermatozoa be present, that they move in an optimal manner and that their plasma membrane be free of major defects are important qualities towards achieving fertilization. However, most ART clinicians are now recognizing that when considered alone, the present criteria (i.e., sperm count, morphology and motility) are of limited predictive value. Often overlooked, the genetic quality and integrity of both the male and female gametes together represent a critical and fundamental parameter towards achieving reproductive success.

It is well understood that both the male and female genetic moieties will govern embryonic development and, at least partly, determine the wellness of the resulting child. However, the relative impact of compromised gametic nuclear integrity on such processes is not equally shared by the parents. As a metabolically active cell, the oocyte possesses all necessary activities to repair and maintain its nuclear compartment. On the contrary, mammalian sperm have evolved such that when reaching full maturity, the cells are totally silent, devoid of cytoplasmic activities and an inherent inability to counteract nuclear DNA alterations, wherever they may result from. Small cell size and high levels of chromatin compaction are further example of physical traits which deprive sperm DNA from normal repair mechanisms (2). Consequently, any DNA damage suffered, especially at the post-testicular stage, whether *in vivo* or *in vitro*, will not inhibit a sperm's fertilization capacity but will get carried through. Following fertilization, the oocyte is then tasked with repairing and correcting all damages harbored by the sperm nucleus upon decondensation and largely prior to the first division of segmentation. Therefore, the risk of incomplete or erroneous repair leading to abortive processes and/or the transmission of defective paternal genetic material to the progeny becomes highly dependent on the level of sperm DNA damage and the efficacy of the oocyte repair system. Additionally, high levels of DNA damage may overwhelm the oocyte repair machinery as an increased number of sites requiring repair increases the likelihood of errors which will also eventually lead to the transmission of *de novo* mutations to the offspring.

Alterations to sperm DNA are very common, arising from a number of physiological and environmental risk factors. Epididymitis or other infection/inflammatory conditions of the male genital tract, exposure to physical and chemical stressors, failing cellular protective activities usually associated with aging, unbalanced diets, varicocele (as indicated by the Agarwal manuscript) are but a few examples of such factors which expose sperm DNA to elevated risk of damage.

As pointed out by the author, there are a number of assays now available which provide a direct or indirect evaluation of sperm nuclear/DNA integrity. New assays evaluating the level of oxidative DNA damage, a largely

underestimated sperm DNA alteration, are also currently being developed. It should be of utmost importance to all ART clinicians to better understand the correlations of sperm DNA integrity with reproductive success and what genetic risks/implications there are in using sperm with altered DNA in ART, especially with the most invasive techniques. As the author indicates, it is now time to incorporate some of these assays in the routine sperm assessment checklist. It therefore also logically follows that when possible, therapeutic strategies aimed at reducing the level of nuclear/DNA damage are pursued prior to ART.

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Footnote

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References

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