Dr. Drevet in his commentary (1) responding to the practice recommendations for Sperm DNA Fragmentation (SDF) testing based on clinical scenarios by Agarwal et al. (2) elegantly discussed the biological effect of DNA fragmentation and its implications to the paternal contribution of the male gamete. The author goes further by elaborating on the likely result of the interactions between sperm with damaged DNA and oocytes with different DNA repair capability.

We concur with the author that the integrity of sperm DNA is crucial for normal fertilization, embryo development, and successful implantation. Evidence indicates that the main pathways leading to SDF occur during sperm transport through the seminiferous tubules and epididymis transit (3). In fact, chromatin compaction is still ongoing during epididymal transit, making it vulnerable to excessive reactive oxygen species (ROS) generated in the epithelial cells of epididymis under physicochemical stressors (4,5). As endonucleases may cleave DNA of mature live sperm (6), sperm DNA damage may ensue through distinct pathways, including hydroxyl radical, nitric oxide, and activation of sperm caspases and endonucleases, thus explaining the high rates of SDF in live ejaculated sperm.

In these conditions, SDF may result from excessive ROS production by spermatozoa themselves in response to a more prolonged epididymal transit and infiltrate polymorphonuclear leukocytes.

Lastly, Dr. Drevet highlights an important take-home message: that despite providing only a global assessment of DNA fragmentation level (without specific information about the severity of DNA fragmentation—single or double strand breaks—and the sites of breaks—intron or exon), the test result is enough for counseling about ART success and genetic risks that may exist following fertilization with such DNA-damaged spermatozoa. Dr. Drevet’s observations suggest that SDF reflects the overall quality of the whole specimen that goes beyond the fragmented sperm detected by the test result. While most studies exploring the predictive ability of SDF testing for pregnancy have measured SDF in the neat semen [reviewed by Esteves et al. (12)], the predictive ability of sperm DNA fragmentation in the post-processing specimens (for use in ART) warrants further investigation.

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None.

**Footnote**

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References

1. Drevet JR. Sperm DNA integrity testing: a valuable addition to the tool box of infertility clinicians. Transl Androl Urol 2017;6:S590-1.

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