Epilogue

The study of sperm DNA and chromatin abnormalities has gained significant importance in the past several years, largely due to the major advances in assisted reproductive technologies (ARTs). Studies in this field have demonstrated that the genetic integrity of the sperm is a key aspect of the paternal contribution to the offspring, particularly, in the context of ARTs. We are now starting to better understand the unique organization of the sperm chromatin, as well as, the nature and etiology of sperm DNA damage.

In Chap. 1 of the textbook, Dr. Rod Balhorn, a pioneer in the field of sperm chromatin structure, describes the dramatic transformation of the physical and functional state of the chromatin during spermiogenesis. A more detailed description of the nuclear proteins and chromatin structure is presented by Dr. Steven Ward and Dr. Raphael Oliva’s group in Chaps. 2 and 3, respectively. These chapters provide us with a better understanding of the unique organization of the sperm chromatin but also show that there are still many unanswered questions about its structure.

The laboratory evaluation of sperm DNA tests is discussed by experts in the field in Chaps. 4, 5, 6, 7, 8, and 9. The authors present us with a detailed description of the SCSA (Dr. Evenson), TUNEL assay (Drs. Muratori and Baldi), benchtop flow cytometer TUNEL assay (Dr. Agarwal et al.), comet assay (Dr. Cortes-Gutierrez et al.), sperm chromatin dispersion assay (Jaime Gosalvez et al.), and cytochemical tests (Dr. Juris Erenpreiss et al.). A broader review of these tests is presented in Chap. 10 (Dr. Tanrikut et al.), and it is concluded that no one test is deemed the optimal assay in the assessment of male infertility.

The etiology of sperm DNA damage is thought to be multifactorial, with the understanding that both primary testicular and secondary (external and post-testicular) factors are involved in its pathogenesis. The putative primary factors responsible for sperm chromatin and DNA damage (oxidative stress (Dr. Henkel et al.), abortive apoptosis (Dr. Sakkas et al.), defective DNA repair (Dr. Boissonneault et al.), and defective spermatogenesis (Drs. Sharma and Agarwal)) are presented in Chaps. 11, 12, 13, and 14. A number of the better known external factors involved in the pathogenesis of sperm DNA damage are discussed in Chaps. 15, 16, and 17.
(lifestyle factors (Dr. Harlev et al.), cancer (Drs. Chan and Robaire), and environmental factors (Drs. Giwercman and Spano)). The role of the oocyte in the repair of sperm DNA damage is presented in Chap. 18 (Drs. Gunes and Sertyel).

The impact of sperm DNA damage on reproductive outcomes and the clinical utility of sperm DNA tests are topics of ongoing debate. In Chap. 19, Dr. Gutierrez-Adan et al. demonstrate from the results of their experimental (animal) studies that sperm DNA damage clearly has a negative impact on reproductive outcomes. In Chaps. 20, 21, and 22, the influence of sperm DNA and chromatin damage on human reproduction are presented (natural pregnancy (Drs. Spanò and Giwercman), ART pregnancy (Drs. Bungum and Oleszczuk), pregnancy loss (Dr. Samanta et al.)). In Chaps. 23 and 24, the pros (Dr. Zini et al.) and cons (Dr. Sigman et al.) of sperm DNA tests in the assessment of male infertility are discussed. These chapters illustrate the strengths and weaknesses of the available studies on sperm DNA damage and human reproduction. The factors responsible for the limited acceptance of sperm DNA tests in the evaluation of infertile men include the marked heterogeneity of clinical studies, the incomplete understanding of sperm chromatin and DNA damage, the lack of standardized sperm DNA test protocols, and the biological variability of these assays.

There are several treatment options for men with sperm DNA damage. Non-specific treatments are discussed in Chaps. 25 (antioxidant therapy, Dr. Agarwal et al.), 27 (physiological ICSI, Dr. Tavaalee et al.), 28 (advanced sperm processing techniques, Dr. Agarwal et al.), and 31 (strategies to diminish DNA damage, Dr. Esteves et al.). In Chap. 26, Dr. Esteves et al. discuss the influence of varicocele on sperm DNA damage and the beneficial effect of varicocelectomy on sperm DNA damage. The potential value of using testicular rather than ejaculated sperm for ICSI in men with sperm DNA damage is debated in Chaps. 29 (pro, Dr. Esteves et al.) and 30 (con, Dr. Chan).

We have made great advances in our understanding of the organization of the sperm chromatin, the etiology of sperm DNA damage, and the potential influence of sperm DNA damage on reproduction. However, several important clinical and biological uncertainties remain. Future studies should be aimed at improving our knowledge of what the various sperm DNA tests measure. Sperm DNA assay protocols should be standardized such that they can provide reproducible results across different laboratories. Future clinical studies evaluating the relationship between sperm DNA damage and reproductive outcomes should be designed as prospective, controlled trials with well-defined populations. These studies will help establish validated and clinically relevant sperm DNA damage thresholds. These steps will surely help address the often heard criticism of the lack of sufficient high-grade evidence in support of the routine use of sperm DNA damage testing in specific clinical scenarios. Ultimately, we hope to establish the clinical value of sperm DNA tests as markers of male fertility potential and develop sound treatment options for infertile men.

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