

Editorial Commentary

Géraldine Delbes, Barbara F. Hales, Bernard Robaire. Effects of the chemotherapy cocktail used to treat testicular cancer on sperm chromatin integrity. *J Androl.* 2007;28:250–251.

The article by Delbes, Hales, and Robaire is a timely contribution on a subject that is becoming a central issue in reproductive medicine, namely the factors that may adversely influence sperm quality and their incidence on fertility, pregnancy, and health of the offspring. By developing and studying an animal model for the influence of chemotherapy (CT) on sperm chromatin integrity, the authors provide a way of testing the influence of different sperm parameters on reproductive competence. They also present experimental support to the notion that testicular cancer treatment can disrupt spermatogenesis and affect sperm quality. Experimental use of the co-administration of bleomycin, etoposide, and cisplatin (BEP) treatment in doses related to the ones used in testicular cancer patients induces DNA strand breaks and increments the susceptibility of sperm to DNA denaturation as studied by the acridine orange assay. It is noted that while these alterations do not compromise fertility in experimental animals, they might be responsible for early death of newborn pups sired by treated male rats, as demonstrated in a previous study (Bieber et al, 2006). These results coincide with similar reports of sperm aneuploidies, spontaneous abortions, and stillbirths in testicular cancer patients treated with CT (De Mas et al, 2001).

The correct identification of alterations in sperm quality are currently relevant because the introduction of ICSI has demonstrated that while immotile or abnormal spermatozoa can successfully fertilize oocytes, it is more and more recognized that poor sperm quality can adversely affect embryo development, implantation and early pregnancy. In this context, the finding that CT can affect chromatin integrity is significant because of the (partial?) recovery of sperm production that follows cancer treatment. As commented in this paper, approximately 80% of testicular cancer patients recover some degree of sperm production after long-term evolution. Most papers dealing with this subject evaluate recovery in terms of sperm concentration and usually do not take

into account other sperm variables, like morphology and motility, that are frequently affected. This is important because oncologists tend to comment on the high recovery rate of patients after CT, while the study of their sperm shows that it is of suboptimal quality. Various publications have reported on structural and numerical chromosome abnormalities in these patients, with frequently contradictory results (Fossa et al, 1994; Martin, 1998; Thomas et al, 2004). Hopefully, new studies comprising larger series of patients may clarify the topic of the long-term effects of CT on sperm quality, which is pertinent when advising patients on the use of contraceptive methods while sperm quality is still compromised.

In the present model the effects of CT are investigated on previously healthy animals, so the interaction of BEP treatment with known deleterious influences of testicular cancer on spermatogenic function cannot be explored. One important aspect when analyzing deleterious influences of CT on patients suffering from testicular cancer is that the disease itself appears to result from previous developmental alterations of testicular function. The fact is that sperm quality in cancer patients treated with CT may depend as much on the deleterious action of CT on chromatin integrity as it depends on previous deterioration of spermatogenesis as part of what Skakkebaek calls the “testicular dysgenesis syndrome” (Petersen et al, 1998, 1999; Hallak et al 1999). This condition comprises a series of testicular pathologies resulting from genetic or environmental alterations in testicular embryonic development. Cryptorchidism, gonadal dysgenesis in intersex individuals, male infertility, and testicular cancer are all conditions that share a common biologic, epidemiologic and environmental background.

While male infertility seems to be on the rise in different parts of the world, the quality of life of human populations, including survivors of testicular cancer, shows considerable improvements, and with this the need to have a healthy offspring. The correct identification and adequate management of the consequences of CT on male fertility are an important issue to which

the paper by Delbes, Hales, and Robaire makes a significant contribution.

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