

Comments in response to Baker KC et al. *F S Rep* 2022;3:110



A recent article in *F&S Reports* by Baker et al., “Poor reproducibility of percentage of normally shaped sperm using the World Health Organization Fifth Edition strict grading criteria,” brought to mind some of our relevant prior work. During a discussion a number of years ago at an Andrology Society meeting, we remarked how the field of andrology was still in the dark ages. If we were hematologists, no one would be satisfied with a descriptive diagnosis, such as microcytic anemia, but want to know the etiology. Was it nutritional, such as iron deficiency, or genetic, such as thalassemia? “Teratospermia” is not a diagnosis but only a description of cells. Abnormalities of the sperm shape have been associated with fever, exogenous heat exposure, varicoceles, cigarette smoking, and exposure to polychlorinated biphenyls. Experimental evidence has also been found in mice of gene mutations that lead teratospermia, which may also occur in humans (1, 2).

We wondered whether abnormalities of the sperm shape caused by these different possible etiologies may lead to variation in the expression of receptors or ligands by spermatozoa that play a role in fertilization, leading to different functional impairments in their ability to interact with the egg or its vestments (3). We tested this hypothesis using zona-free hamster eggs, which could be penetrated by human sperm, but only after they had undergone capacitation and an acrosome reaction, steps that occur in homologous in vitro fertilization of human eggs (4).

In men exhibiting severe teratospermia, an abnormal sperm shape was associated with impaired egg penetration. However, the functional impairments of sperm differed in different men. In some cases, sperm failed to adhere to the

hamster egg oolemma, and in other cases, sperm adhered but did not penetrate the eggs; on the other hand, sperm from other men with teratospermia behaved normally and entered the cortical ooplasm despite their abnormal appearance (5).

Our findings may explain the varying, divergent effects of teratospermia on pregnancy rates referenced in Baker et al., beyond the rigor of laboratory quality control and reliability of the assessment of the sperm shape. Perhaps it is time, despite the availability of intracytoplasmic sperm injection, to refocus on learning how the spermatozoon enters the oocyte and how that process may be impaired by abnormalities in spermiogenesis.

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