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Commentary

A clinical assay for reactive oxygen species – ready for primetime?

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Abstract

Reactive oxygen species (ROS) have been demonstrated to have damaging effects on human sperm function. The measurement of ROS as an adjunct to traditional semen analysis has clinical relevance as part of the diagnosis of male infertility. The assay best suited to the clinical laboratory environment for detecting ROS generation remains somewhat controversial. A recent report on a multicenter study evaluating the reduction of nitroblue tetrazolium (NBT) to formazan precipitate as an indirect reporter of ROS-generating activity in spermatozoa, seminal plasma and semen has received a critique raising questions as to the sensitivity and specificity of the assay for detecting ROS. The authors of the report argue in response that the assay has validity and yields results that are potentially clinically significant. This dialogue serves to (re)direct readers to the original article and to consider carefully the intent and potential application of the assay, and whether there is sufficient scientific evidence to judiciously support its clinical diagnostic application.

Keywords: reactive oxygen species; ROS; sperm function; semen analysis; nitroblue tetrazolium; NBT

The traditional semen analysis has, arguably, limited predictive value for pregnancy and, as a consequence, adjunct sperm tests have been developed to augment clinical decision making for infertility treatment. One putative adjunct test is the measurement of reactive oxygen species (ROS).

In a landmark publication, Aitken and Clarkson (1987) demonstrated that washed human spermatozoa generated ROS in response to treatment with a calcium ionophore, A23187. Further, they found variation amongst subject specimens in response to ionophore, with some specimens producing a dramatically higher release of ROS than others. Significantly, the greater the burst of ROS in response to ionophore treatment, the poorer the fusion of those sperm with zona-free hamster oocytes. Collectively, the data reveal that elevated concentrations of ROS negatively impact on critical aspects of human sperm function.

In a subsequent study, Aitken and Clarkson (1988) published data that transformed the way in which semen samples are processed in the clinical andrology laboratory. They found that techniques that selected motile from poorly motile sperm populations prior to centrifugation, such as density gradient centrifugation (DGC) or direct swim up, produced a highly functional suspension of sperm as demonstrated by high percentages of both motility and ionophore-induced sperm-oocyte fusion. In contrast, if semen samples were processed without such a preselection technique, then the functional ability of motile spermatozoa was diminished and

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