

Seminal Total Antioxidant Capacity Identifies Infertile Men Cleveland Clinic establishes TAC reference value

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Development of a simple colorimetric assay that discriminates proven fertile from infertile men based on total antioxidant capacity (TAC) holds promise as a diagnostic and prognostic tool in the management of male infertility. Our research has established the normal range for seminal plasma TAC to differentiate infertile from fertile men.

Male factor infertility accounts for 30 to 50 percent of all infertility. Defective spermatozoal function is the most common cause of male infertility, resulting from testicular pathologies; genetic disorders; exposure to drugs, toxins or irradiations; or oxidative stress.

Oxidative stress results when levels of reactive oxygen species (ROS) exceed the available total antioxidant capacity. An increase in seminal ROS levels without a concomitant rise in antioxidant defenses leads to oxidative stress, which can cause damage to the spermatozoa, oocyte and embryo. Through the work of our laboratory and other leading infertility centers worldwide, the role of oxidative stress in the pathogenesis of male and female infertility and the failure of assisted reproductive techniques is now widely recognized.

Under normal conditions, seminal plasma has a very effective antioxidant system that provides the spermatozoa with a protective environment against oxidative stress. This system involves a combination of enzymatic (e.g., superoxide dismutase, catalase and glutathione peroxidase) and nonenzymatic (e.g., ascorbate, urate, vitamin E, pyruvate, glutathione, taurine, and hypotaurine) antioxidants that are very efficient under normal conditions in scavenging reactive oxygen species to maintain homeostasis in the cellular environment. This system breaks down under conditions that cause an excess of ROS or depletion of antioxidant levels.

Seminal total antioxidant capacity (TAC) is a measure of the seminal plasma's ability to scavenge ROS and prevent oxidative stress. Several reports relate low seminal plasma TAC levels to male infertility, as well as in embryo culture media from the oocytes, cumulus cell mass, and spermatozoa used for insemination in conventional *in vitro* fertilization. The potential cellular sources of TAC in an intracytoplasmic sperm injection setting are the spermatozoa and the injected oocytes.

From the clinical perspective, an accurate assessment of the patient's TAC is an important factor in the diagnosis and management of male infertility. Seminal TAC can be measured as the total available antioxidant protection in the seminal plasma by a variety of colorimetric assays. TAC measurement by colorimetric assay is simple, rapid and economical.

Key Points:

We recently published a study that identifies a cutoff value for seminal plasma TAC level that can differentiate infertile from fertile men with high sensitivity (76%) and specificity (64%) of the test and low operator variability.

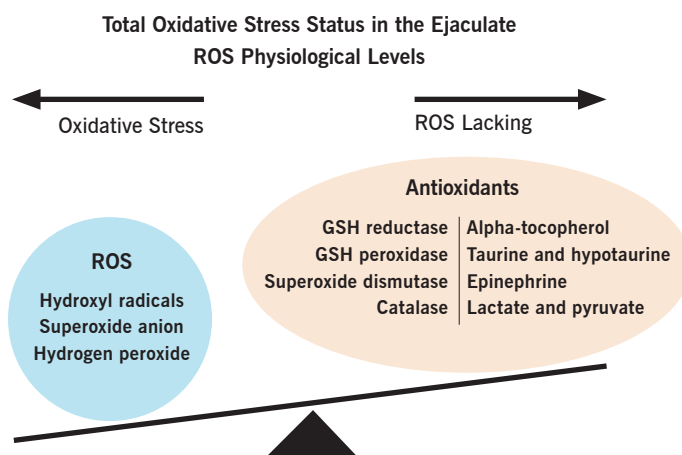
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Despite the availability of an assay for TAC, studies have established a normal reference range. We recently published a study that identifies a cutoff value for seminal plasma TAC level that can differentiate infertile from fertile men with high sensitivity (76%) and specificity (64%) and low operator variability.

In our study, the infertile patient group showed lower seminal plasma TAC levels compared to both the proven fertile and the sperm donor groups. We established the cutoff value of 1,420 micromoles of Trolox for seminal plasma TAC.

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We recommend further studies to establish reference values for different clinical diagnoses of male infertility such as varicocele and infection as well as conditions related to poor semen parameters such as hyperviscosity and varying abstinence periods. Ongoing research using this assay may allow targeted antioxidant and other therapies to restore fertility. ■



Delicate balance between the formation of reactive oxygen species and the scavenging mechanism of the various enzymatic and nonenzymatic antioxidants. An imbalance between the two results in oxidative stress.