SPERM DNA DAMAGE

DNA damages present in sperms after specialized type of cell division but before fertilization which can be repaired in the fertilized egg.

⚠️ Risk factor ♂ Male

About Sperm DNA Damage

Human spermatozoa are particularly vulnerable to free radical attack and the generation of oxidative DNA damage which include DNA fragmentation (the separation or breaking of DNA strands into pieces).

It is generally accepted that oxidative stress (OS) is an important factor in male infertility because it may impair the physiological function of spermatozoa at the molecular level. Nevertheless, although several approaches have been reported, the imbalance between production of reactive oxygen species (ROS) and activity of the antioxidant defense system in semen is difficult to investigate and remains poorly understood.

Reactive oxygen and reactive nitrogen species (ROS and RNS), a group of highly reactive oxidants, most of which contain unpaired electrons, are usually known as ROS or free radicals. At physiological levels they have important roles in metabolism in all aerobic organisms. However, excessive ROS production which can not be effectively controlled by antioxidants leads to oxidative stress (OS) which has been linked to many pathological processes, including male infertility. Standard semen analysis is often inadequate to explain conception failure as the routine microscopic evaluation can not reveal subtle disorders at the molecular level which may be caused by OS. This situation often leads to diagnosis of idiopathic infertility. Moreover, there is some degree of overlap in sperm parameters between fertile and infertile males.

Leukocytes (polymorphonuclear neutrophils and macrophages) have important implications in male fertility in that they produce reactive oxygen species (ROS). Leukocytes contribute directly and indirectly to reactive oxygen species (ROS) production. Although leukocytospermia (presence of leukocytes in ejaculate) is defined as the presence of ≥1 × 106 white blood cells/mL (WBC/mL) in a semen sample, the presence of less than 1×106WBC/mL (low-level leukocytospermia) can still produce a detectable amount of ROS, impairing sperm function and lowering the chances of pregnancy.

Symptoms
- infertility

Associated diseases
- no associated diseases

Complications
- infertility

Risk factors

Many environmental, physiological, and genetic factors have been implicated in the poor sperm functions and infertility. Thus, it is very important to identify the factors/conditions which affect normal sperm functions. The most dangerous factors which leads to creation of ROS are smoking and alcohol drinking.

Prevention
ROS levels and DNA damage were significantly increased in patients with low-level leukocytospermia. There is an important implication to even a reduced number of leukocytes in the semen. Low-level leukocytospermia is pathological and that treatment should be considered in these individuals in addition to semen cultures for underlying infection. The supplementation of a cryopreservation extender (a liquid diluent which is added to semen to preserve its fertilizing ability) with antioxidant has been shown to provide a cryoprotective effect (a substance used to protect biological tissue from freezing damage) on mammalian sperm quality.

Spermatozoa are protected by various antioxidants and antioxidant enzymes (molecules that inhibit the chemical reaction that can produce free radicals, leading to chain reactions that may damage cells of other molecules) in the seminal plasma or in spermatozoa itself to prevent oxidative damage. An antioxidant that reduces oxidative stress and improves sperm motility could be useful in the management of male infertility. Antioxidants are the agents, which break the oxidative chain reaction, thereby, reduce the oxidative stress. Vitamin E (antioxidant) may directly quench the free radicals, thus it is suggested as major chain breaking antioxidant. Antioxidants, in general, are the compounds and reactions which dispose, scavenge, and suppress the formation of ROS, or oppose their actions. Mn2+ enhances sperm motility, viability, capacitation and acrosome reaction by decreasing the oxidative stress. Thiols groups also play an important role in detoxification and antioxidation of ROS, besides maintaining the intracellular redox status. These groups serve as defense mechanisms of sperm cells to fight against oxidative stress. A variety of biological and chemical antioxidants that attack ROS are presently under investigation. Supplementation with antioxidants during IVF (in vitro fertilization) procedures impaired sperm quality, normal pronuclear formation, and embryo development to the blastocyst stage.

**How it can affect fertility**

In the genital tract, low levels of ROS are necessary for normal function of human spermatozoa, including their

- capacitation (is the step in the maturation of mammalian spermatozoa and is required to render them competent to fertilize an oocyte),
- acrosome reaction (the reaction that occurs in the acrosome of the sperm as it approaches the egg, a sperm must first fuse with the plasma membrane and then penetrate the female egg in order to fertilize it) and
- sperm-oocyte fusion (a process in which two cells combine in one).

On the other hand, excessive OS may cause lipoxygenation of sperm (the oxidative degradation of lipids) membranes resulting in DNA damage and sperm apoptosis (a process of programmed cell death). After gaining entry into the sperm, ROS target genetic materials, destroying mitochondrial DNA and inhibiting intracellular ATP (a nucleoside triphosphate) production. Without proper ATP production, both functionality and sperm motility is affected and fertilization of an egg is not possible.

**Prognosis**

Evaluation of OS and the use of antioxidants are not routine in clinical practice. The immediate need is to simplify and validate the evaluation of ROS and OS status so that it can be performed routinely without the use of sophisticated equipment. Also, it is important to establish reference values for ROS above which antioxidants could be used for male infertility treatment. The dose and duration of these antioxidants should also be determined and standardized.

OS can cause DNA fragmentation. Sperm DNA fragmentation rates have been correlated with sperm viability rates. Reduced sperm viability is associated with high sperm DNA fragmentation, while conversely high sperm viability is associated with low rates of sperm DNA fragmentation. Both elevated DNA fragmentation rates and poor viability are correlated with impaired male fertility, with a DNA fragmentation rate of > 30% indicating subfertility.

Elevated sperm DNA fragmentation rates have been positively correlated with impaired fertility, including longer times to natural conception, impaired embryo cleavage, impaired implantation rates, higher miscarriage rates, and increased risk of pregnancy loss after both in vitro fertilization (IVF) and intracytoplasmic sperm injection (ICSI). Using the sperm chromosome structure assay, couples with a sperm DNA fragmentation have been shown to have greater probability of pregnancy via natural intercourse than those with DNA fragmentation.
Sources

"The relationship between sperm viability and DNA fragmentation rates" — by Samplaski et al. licensed under CC BY 4.0

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"The measurement of reactive oxygen species in human neat semen and in suspended spermatozoa: a comparison" — by Fingerová et al. licensed under CC BY 2.0

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