Sperm DNA fragmentation

The genetic integrity of the spermatozoan is essential for normal embryo development. A high level of DNA fragmentation in sperm cells may represent a cause of male infertility that conventional examinations – sperm concentration, motility analysis, morphology assessment – cannot detect. Results reported in the scientific literature have shown that regardless of the assisted reproductive technology used, an elevated level of DNA fragmentation above the critical threshold will significantly compromise the possibility of a successful pregnancy.

- High sperm DNA fragmentation does not appear to affect fertilisation or the first or second embryo cleavage stages.
- High sperm DNA fragmentation can affect embryo cleavage once the paternal genome is switched on, and subsequent blastocyst development.
- DNA fragmentation levels are closely correlated with IUI, IVF and ICSI miscarriage and pregnancy rates.
- DNA fragmentation is significantly higher in subfertile men.
- Men with poor semen parameters are more likely to have high DNA fragmentation.
- High sperm DNA fragmentation is also found in men with normal semen parameters.

Advantages of the Sperm DNA Fragmentation test

This test provides a reliable analysis of sperm DNA integrity that may help to identify men who are at risk of failing to initiate a healthy ongoing pregnancy. Information about sperm DNA integrity may help in the clinical diagnosis, management and treatment of male infertility and may be of prognostic value in assessing outcome of assisted conception treatment.

High rates of Sperm DNA Fragmentation and pregnancy

Normal, healthy pregnancies do occur in couples where the male partner has a high percentage of sperm with fragmented DNA, although the chances are significantly reduced, as the percentage of sperm bearing low levels of DNA fragmentation is much lower. Embryos derived from sperm whose DNA is highly fragmented have a poor prognosis. Evidence suggests that this could result in initiation of apoptosis and mutations resulting in blastocyst arrest, miscarriage, abnormalities in the offspring and an increased susceptibility to childhood cancer. Protection against high DNA fragmentation may be afforded by younger oocytes which are much more efficient at DNA repair of defective sperm than older oocytes, so a couple coming for assisted conception treatment where the sperm DNA fragmentation level is high has a better prognosis if his partner is young.

Causes of Sperm DNA Fragmentation

A major causative factor for sperm DNA damage is oxidative stress. Other factors include abnormalities in the regulation of apoptosis, or defects in topoisomerase activity. Increased sperm DNA fragmentation is associated with:

- Infection
- Leucocytospermia
- Sperm cytoplasmic droplets
- Febrile illness
- Elevated testicular temperature
- Diet
- Drug use
- Cigarette smoking
- Exposure to environmental and occupational pollutants
- Advanced age
- Varicocele

Indications for male patients who may benefit from the test

- Unexplained infertility
- Arrested embryo development
- Poor blastocyst development
- Multiple failed IVF/ICSI treatment
- Recurrent miscarriage in partner
- Advanced age
- Varicocele
- Poor semen parameters
- Exposure to harmful substances
Treatment

Some causes of DNA fragmentation cannot be treated, but if the damage is caused by free radicals, then a change in lifestyle and a diet designed to protect against oxidative stress may help reduce the levels of DNA fragmentation in some of these cases. Treatment of infection with antibiotics would also be expected to reduce DNA fragmentation. There is some evidence to show that varicocele repair may improve sperm DNA integrity. Initiatives to reduce the levels of fragmentation can be assessed by undertaking a second test three months after the first. Initial reports suggest that DNA damage occurs at the post-testicular level, so that testicular sperm may have a healthier DNA integrity than ejaculated sperm. Furthermore, studies show that ICSI may be a more effective treatment than IVF for sperm with a high DNA fragmentation.

What is the DNA fragmentation test?

This test is an effective method for measuring thousands of sperm in an ejaculate. Sperm are stained with a fluorescent probe that interacts with the DNA molecule. The fluorescence signal changes when the DNA is fragmented, and this is monitored using a flow cytometer. The SCSA® test has been developed over the last 20 years and is CLIA approved.

Results

The results are reported showing 3 statistical categories of fertility potential:

DNA Fragmentation Index (%DFI; % sperm cells containing damaged DNA)

≤ 15% DFI = excellent fertility potential

> 15 to < 30% DFI = good fertility potential

≥ 30% DFI = fair to poor fertility potential*

The statistically significant DFI threshold for subfertility has been established at > 30%. Normal full-term pregnancies are possible with an elevated DFI, but the higher the level of fragmentation, the greater the incidence of reduced term pregnancies and miscarriage.

High DNA stainability (HDS; % cells with immature chromatin)

≤ 15% HDS = normal

> 15% HDS = above normal

Immature chromatin can be measured by high DNA stainability (HDS) and is associated with asyngamy and poor IVF fertilisation rates when it exceeds 15%.

REFERENCES


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