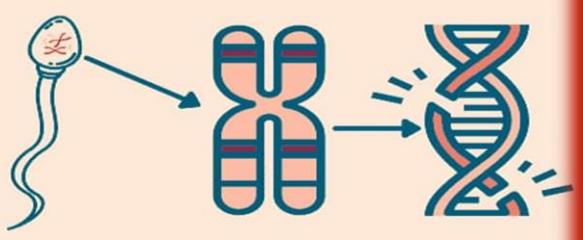


Image 1

DNA FRAGMENTATION IN SPERM

Chaitali Puthran
ASPIER Batch: 2022-24

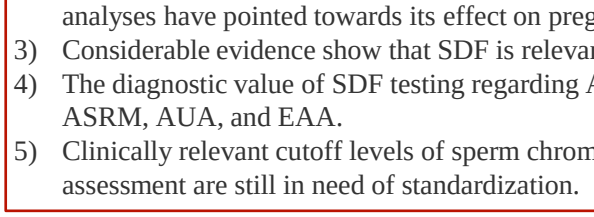
- Sperm DNA fragmentation pertains to the amount of damage observed in sperm DNA, specifically measuring the percentage of sperm with physical breaks in their genetic material.
- Alterations of any kind in sperm DNA are likely to cause infertility in the man affected, as integrity of sperm DNA is key to obtaining viable embryos and subsequently a healthy baby.
- The higher the sperm DNA damage index, the lesser the chances of achieving an ongoing pregnancy.

CLINICAL SIGNIFCANCE

< 20% DFI = Good fertility potential

> 20 to < 30% DFI = Suspicious

> 30% DFI = Clinically significant



CAUSES

Three primary mechanisms can lead to SDF:

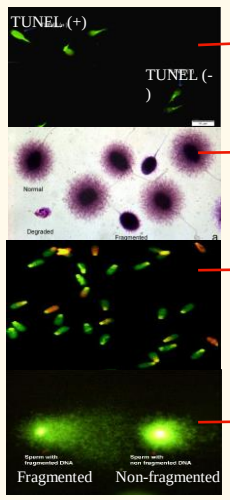
(1) **Abortive apoptosis**, where spermatozoa destined for apoptosis fail to complete the process and are released with fragmented DNA due to the action of endonucleases

(2) **Defective chromatin maturation,** where during the normal process of sperm chromatin compaction, DNA nicks are not repaired, leading to persistent breaks as well as less compact DNA that is more susceptible to damage by exogenous factors

(3) **Oxidative stress,** where reactive oxygen species can directly induce DNA breaks in the testes or as spermatozoa move along the male reproductive tract

(4) Damage to the sperm DNA can occur within the testes, during passage along the reproductive ducts, after ejaculation during sperm processing, or during cryopreservation.

TESTS TO MEASURE DNA FRAGMENTATION



(1) **Terminal deoxynucleotidyl transferase dUTP nick end labelling (TUNEL) assay** which adds a labelled nucleotide to sites of DNA nicks and later assess extent of fluorescence

(2) **Sperm chromatin dispersion (SCD) test** which relies on formation of a halo by intact DNA around the nucleus after denaturation and a smaller or absent halo with fragmented DNA

(3) **Sperm chromatin structure assay (SCSA)** which uses Acridine orange (AO) and measures the DFI, defined as the ratio between red fluorescence (AO bound to single stranded DNA at sites of breaks) and green fluorescence (AO bound to double stranded intact DNA)

(4) **Comet assay** which is a single cell electrophoresis in which fragmented DNA forms a tail while intact DNA remains in the comet head

CONSEQUENCES

- Reduced fertility
- Reduced embryo development and quality
- Lower pregnancy rates
- Higher risk of genetic abnormalities
- Poorer embryo implantation and miscarriage
- Increased risk of childhood health issues

MANAGEMENT

1. Lifestyle modifications
quit smoking and drinking, engage in exercise and manage weight, wear loose underwear, avoid high temperature workspaces and environment and abstain from ejaculation for an appropriate duration

2. Infection control
medication for 2–12 weeks to decrease the amount of reactive oxygen species produced by the white blood cells

3. Oral antioxidant therapy
Antioxidants, vitamin E, vitamin C, selenium, coenzyme Q10, N-acetylcysteine, zinc, and L-carnitine, pyruvate, taurine, hypo taurine.

4. Varicocele repair by varicocelectomy

5. Micromanipulation-based sperm selection
Density gradient centrifugation, electrophoretic sperm isolation using a cell sorter, a hyaluronic acid-binding method, sperm magnetic sorting, and high-magnification microscopy.

6. Sperm processing and preparation
Conventional (swim up, DGC) techniques, Magnetic Activated cell sorting (MACS), Intracytoplasmic morphologically selected sperm injection (IMSI). Other approaches include the physiological intracytoplasmic sperm injection (PICSI), microfluidic devices.

7. Use of testicular sperm for intracytoplasmic sperm injection

SDF TESTING AND INFERTILITY

1) Several papers have been published presenting the usefulness of SDF Test in assessing male fertility
2) There is an ongoing debate regarding the use of SDF as part of the standard tests, although various meta-analyses have pointed towards its effect on pregnancy, miscarriage, and live birth.
3) Considerable evidence show that SDF is relevant in the context of evaluation prior to ART
4) The diagnostic value of SDF testing regarding ART outcomes has recently been recognized by WHO, ASRM, AUA, and EAA.
5) Clinically relevant cutoff levels of sperm chromatin integrity and the optimal techniques for SDF assessment are still in need of standardization.

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