INTERNATIONAL HUMAN EMBRYOLOGY RESEARCH ACADEMY

AndroNet
An Initiative of IHERA

# AndroDigest

## The Science of Fatherhood

*Rewriting the Narrative of Fatherhood Through Science and Awareness*

### Featured in this Issue

- Male infertility – basics and stats
- Management of male infertility
- Myths Vs Facts : Sperm DNA Fragmentation Index
- Research spotlight

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## About AndroDigest

**AndroDigest**, as a first Newsletter under the initiative of AndroNet, represents a significant step toward making our vision, a reality.

AndroDigest is a thoughtfully curated newsletter dedicated exclusively to male reproductive health. Each issue is designed to break down recent research, emerging trends, and key concepts into concise, easy-to-understand insights. The focus is not just on presenting information, but on translating it into practical knowledge that can be readily applied in clinical and laboratory settings.

Every edition of AndroDigest aims to provide:

- **Simplified summaries of recent research**
- **Clinical and laboratory relevance of new findings**
- **Expert perspectives and interpretations**
- **Practical takeaways for daily practice**
- **Updates on evolving techniques and technologies in andrology and embryology**

Whether it is understanding sperm function tests, interpreting advanced diagnostics, improving laboratory outcomes, or staying updated with innovations in assisted reproduction, AndroDigest serves as a reliable and accessible resource.

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## Vision & Future Direction

AndroNet envisions building a strong knowledge-sharing platform that goes beyond a newsletter. Future initiatives may include educational modules, expert discussions, workshops, and collaborative learning opportunities aimed at strengthening the field of male fertility.

Through AndroDigest and upcoming initiatives, AndroNet aspires to create a community where science is shared openly, understood clearly, and applied effectively — ultimately contributing to better reproductive health outcomes.

# Understanding Male Infertility

**Male infertility — basics and stats**

**How common is it?**

Infertility is usually defined as failure to conceive after 12 months of regular, unprotected intercourse and affects about **8–12% of couples worldwide**, with a **male factor present in ~50%** of infertile couples. Many guidelines cite a practical prevalence of **~1 in 6 couples**, reflecting region- and method-dependent estimates.

**Key definitions.**
*Primary infertility* refers to couples who have never conceived.

*Secondary infertility* applies when a pregnancy occurred previously but is not occurring now. Clinicians also distinguish U*nexplained infertility* (normal semen parameters and normal partner evaluation) from *Idiopathic male infertility* (abnormal semen parameters without a defined cause), a distinction that guides testing and counselling.

**Why does male infertility occur?**

Etiologies include congenital or acquired urogenital abnormalities, genital tract infections, **varicocele**, endocrine disorders, immunologic factors, and iatrogenic or environmental exposures. Modifiable risks—**obesity/metabolic syndrome, smoking and alcohol, scrotal/occupational heat, and environmental toxins/air pollution**—are consistently associated with poorer semen quality or reproductive outcomes.

**First-line evaluation—parallel and structured.**

Current AUA (American Urological Association)/ASRM (American Society of Reproductive Medicine) guidance stresses evaluating **both partners in parallel** to avoid unnecessary or invasive interventions and to direct the least invasive effective therapy. The cornerstone test is a **WHO 6th-edition semen analysis** performed with standardised methods and quality control; the 6th edition re-emphasizes motility sub-categories, strict morphology, vitality, and robust reporting to improve inter-lab comparability. Because of biological and technical variability, **abnormal results should be repeated** before management decisions are finalized.

**Sperm DNA fragmentation (DFI/SDF) and oxidative stress.**

Elevated SDF reflects DNA breaks and chromatin instability, often driven by **oxidative stress** (excess reactive oxygen species). Higher SDF is linked to **lower fertilisation**, **slower embryo morpho kinetics**, and **poorer blastocyst quality** in IVF/ICSI cohorts; effects on clinical pregnancy or live birth are more variable between studies. Accordingly, SDF is an **extended (non-routine) test**—best reserved for recurrent ART failure, recurrent pregnancy loss, unexplained infertility, or clinical varicocele—using validated assays with **assay-specific cut-offs** and standardised pre-analytics.

**Hormones, imaging, and genetics (targeted).**

A **targeted endocrine profile** (FSH, LH, total testosterone ± prolactin) helps differentiate primary testicular failure from hypothalamic–pituitary causes and guides therapy or referral. **Scrotal Doppler ultrasound** is useful when the physical exam is equivocal (e.g., staging a suspected varicocele) or to assess intratesticular/epididymal pathology, but it complements rather than replaces a hands-on exam. **Genetic testing** is phenotype-driven karyotype and Y-chromosome microdeletions for azoospermia or severe Oligozoospermia, and **CFTR** analysis in suspected congenital bilateral absence of the vas deferens.

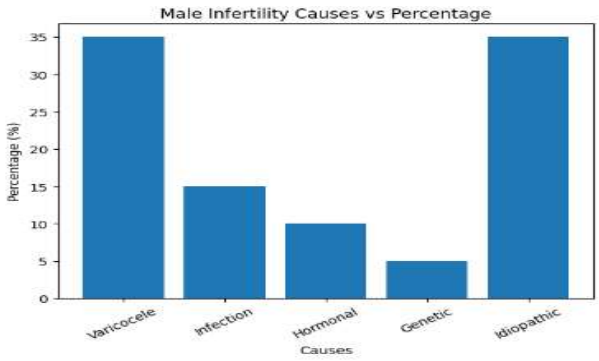
**Management—start with the reversible.**

Lifestyle optimization (weight management, smoking cessation, reducing heat/toxin exposure) and treatment of correctable conditions (e.g., infection) are first-line and often improve semen parameters or readiness for ART. **Varicocele** is the most common surgically correctable cause; repair is recommended for infertile men with a **palpable varicocele and abnormal semen parameters**, with shared decision-making when SDF is high despite borderline routine parameters. When indicated, assisted reproductive techniques—**IUI, IVF, ICSI**—are effective pathways to pregnancy, selected according to both partners' findings, prior response, and the couple's goals and timeline.

**Take-home for clinics and couples.**

1. Male infertility is **common and multifactorial**; a male factor is present in about half of infertile couples.
2. Use **WHO-standard semen analysis** and **repeat** abnormal results; add **targeted** tests (SDF, endocrine, imaging, genetics) based on presentation.
3. **Prioritise reversible factors** (lifestyle, varicocele, infections), integrate female-factor data, and choose the **least invasive effective** pathway, reserving ART for appropriate indications

World Health Organization, 2021 (WHO Manual 6th Edition) | American Society for Reproductive Medicine Practice Committee, 2020




## Awareness Tools • Patient Education.

### Semen analysis is a simple first test of male fertility.

**Prepare**: Abstain 2–5 days; avoid lubricants unless sperm-safe; note recent fever/medications.
**Collect**: Masturbate into a sterile container (ideally at clinic). If at home, deliver within 1 hour, kept near body temperature; collect the entire sample.
**Measures**: Volume, concentration (count), motility, morphology.
**Results**: Vary—two tests are often advised. Values below reference ranges don't rule out natural conception; your clinician will interpret and guide next steps.

# Myths Vs Facts – Understanding Male infertility.

**Sperm DNA Fragmentation (DFI) — what clinicians and patients should know**

**Myth 1: "DFI is a routine test for every infertile man."**
**Fact:** DFI/SDF is an *extended* semen assessment to be used **selectively**—for example in recurrent pregnancy loss, recurrent ART failure, unexplained infertility, or clinical varicocele—rather than as first-line screening. The WHO 6th edition lists SDF among extended tests, and AUA/ASRM (2024) emphasizes targeted use as part of a broader evaluation

**Myth 2: "A single DFI value proves male infertility."**
**Fact:** DFI is a **biomarker**, not a standalone diagnosis. It should be interpreted alongside repeated, guideline-standard semen analyses, endocrine and genetic findings, and the female partner's factors

**Myth 3: "DFI only matters for natural conception—ICSI bypasses it."**
**Fact:** Higher DFI correlates with **lower fertilisation, slower embryo morpho kinetics, and poorer blastocyst quality** in IVF/ICSI cohorts. Effects on clinical pregnancy/live birth are variable, but several large studies link higher DFI to **higher miscarriage** and even **lower birthweight**. ICSI does not universally "solve" high DFI.

**Myth 4: "There is a universal DFI cut-off for decision-making."**
**Fact:** Cut-offs are **assay-specific** (TUNEL, SCSA, SCD, Comet) and lab-validated; thresholds should not be transferred across platforms. A recent meta-analysis suggests a **threshold-dependent** relationship with euploidy at higher DFI (≥30%)—another reason to report the assay and context.

**Myth 5: "Oxidative stress and DFI are unrelated."**
**Fact:** Oxidative stress is a **major driver** of sperm DNA damage. Excess ROS induces strand breaks and chromatin disruption; managing ROS sources is central to improving DNA integrity.

**Myth 6: "Any antioxidant plan will fix high DFI."**
**Fact:** Lifestyle optimization (stop smoking, reduce heat/toxins, treat infections) is foundational; evidence for antioxidant **supplements** is mixed and should be individualized and time-limited with follow-up testing.

**Myth 7: "All centrifugation makes DNA damage worse, so avoid DGC."**
**Fact:** Technique matters. **Prolonged/strong centrifugation** can raise ROS (time is a bigger driver than g-force), but well-executed **density-gradient centrifugation (DGC)** can reduce ROS carryover in the motile fraction. Individualize centrifugation times rather than abandoning DGC.

**Myth 8: "Varicocele status doesn't affect DFI."**
**Fact:** Varicocele is associated with **elevated SDF and oxidative stress**. Repair benefits **selected** men (palpable varicocele, infertility, abnormal semen parameters), with shared decision-making when SDF is high despite borderline routine parameters.

**Myth 9: "Testicular sperm is always better than ejaculated sperm if DFI is high."**
**Fact:** Some centres consider testicular sperm in **recurrent failures with persistently high ejaculated DFI**, but this is **not** a one-size-fits-all solution; decisions must weigh risks, female factors, and prior outcomes

# Understanding Male Infertility: Latest Evidence

## Research Spotlight

Oxidative stress— it is an imbalance between reactive oxygen species and antioxidant defences—induces lipid peroxidation and nuclear damage in sperm, leading to **sperm DNA fragmentation (SDF/DFI)** and contributing to male subfertility. SDF is a biomarker of sperm nuclear quality that most guidelines recommend using **selectively**: the WHO 6th edition lists it as an "extended" (non-routine) semen examination, and expert statements/AUA–ASRM updates suggest testing in unexplained infertility, recurrent pregnancy loss, prior ART failure, clinical varicocele, and in men with notable risk of exposures or advanced paternal age. Measurement relies on validated assays (TUNEL, SCSA, SCD, Comet) with assay-specific thresholds and strict pre-analytics; oxidation–reduction potential.

MiOXSYS - can screen for redox imbalance, but its sperm-count–indexed interpretation remains debated. At the bench, elevated DFI is consistently associated with lower fertilisation, slower embryo morpho kinetics, and poorer blastocyst quality, while effects on clinical pregnancy/live birth vary; several large cohorts report higher miscarriage and lower birthweight at higher DFI, indicating a robust embryology-level signal with context-dependent clinical translation. When DFI is high, management focuses on modifiable factors (cessation of smoking/heat and toxin exposure, treatment of infection, lifestyle ± antioxidant strategies with mixed evidence), varicocele repair when indicated, and—in select couples with repeated ART failure—consideration of testicular sperm for ICSI on a case-by-case basis.

### Andro Digest • Expert Micro Opinions

**Reproductive Andrologist/ Urologist**: "Early referral after an abnormal semen analysis shortens time to treatment."

**Embryologist:** "Optimizing gradient preparation and minimizing ROS are lowcost, highimpact wins."

**Counsellor:** "Normalize malefactor conversations; involve partners from day one in couples Fertility journey".

# Understanding Male Infertility: The Fun Way!

**Answer the questions from the crossword**:

1. I help select the best sperm, I bind to hyaluronic acid, Used in ICSI to improve outcomes.

2. Process of sperm formation

3. Cell producing testosterone

4. Hormone stimulating spermatogenesis

5. Tube where sperm matures

6. No sperm seen, Fructose is positive.
   Obstruction or failure to produce, Treatment depends on the root.

7. Genetic material carrier

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**For Crossword answers, please visit www.ihera.org**

# Understanding Male Infertility: The Fun Way!

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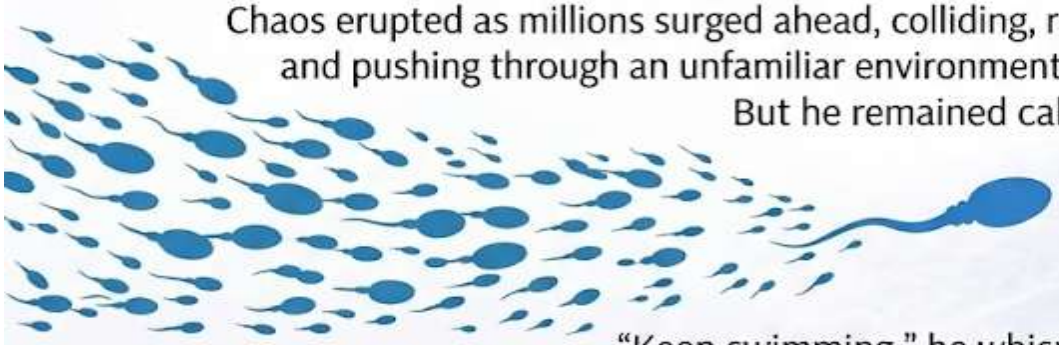
## The Last Swim: A Sperm's Story

A powerful force propelled them into the unknown.
Chaos erupted as millions surged ahead, colliding, racing,
and pushing through an unfamiliar environment.
But he remained calm.



"Keep swimming," he whispered.

The path was harsh and dangerous.
Many slowed, faltered, and disappeared.
The numbers dwindled. What started as a vast army
became a scattered few.

**Still, he swam.**


**Time passed.** The crowd had nearly vanished.
Only a handful remained.

**Then, he saw it—the destination: the egg.**

With one final push, he directed his energy toward this moment. Others tried,
but they fell short. He surged ahead, driven by purpose.

**Among millions, he was the one.**

**Moral:** Like that tiny swimmer, success in life often hinges on staying
focused, moving forward, and making it.