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Male Infertility: Treatment Approach – A Committee Opinion

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INTRODUCTION

Male infertility is a complex and often underdiagnosed condition that contributes to nearly half of all infertility cases (1). Effective treatment requires a comprehensive and individualized approach centered around three main pillars: lifestyle modification, pharmacological intervention, and surgical treatment (1-8). These approaches must be applied individually and may be combined depending on each patient's clinical and laboratory profile. The primary

objectives are to optimize testicular and sperm function, enhance the likelihood of natural conception when feasible, and improve quality of life—given that male infertility is also a biomarker of general health (9-11). Appropriate management also seeks to improve outcomes with assisted reproductive technology (ART) when this treatment modality is indicated (9-11).

Lifestyle Modification

Increasing evidence indicates that infertile men are at higher risk for developing cardiometabolic disorders and have greater cardiovascular and all-cause mortality compared to fertile men (1). They are also more prone to chronic conditions such as obesity, metabolic syndrome, hypogonadism, and cancer.

In the context of couple infertility, an andrological assessment is essential (1). It should be carried out by an andrologist or urologist with expertise in male reproductive health, alongside a fertility specialist's evaluation of the female partner (1, 2, 4, 6-10).

The andrological consultation represents a unique opportunity to identify modifiable risk factors, relevant family history, and early-stage diseases, which may improve fertility, androgen production, and overall health. The testes consist of two main compartments—the hormonal and the spermatogenic—and their proper function directly impacts reproductive and sexual health, quality of life, and longevity (1, 12).

Adopting healthy habits is an essential part of treatment and must include guidance on avoiding or minimizing exposure to risk factors, categorized as follows (1, 4, 6-10, 13-22):

i. General factors: aging, obesity, metabolic syndrome, hypertension, autoimmune diseases, infections of viral (e.g., mumps, COVID-19) or bacterial origin, and cancer.

ii. Lifestyle factors: poor diet, excessive alcohol consumption, recreational drug use (e.g., cannabis), smoking (including electronic cigarettes and vaping), sedentary behavior, prolonged exposure to electromagnetic radiation (e.g., mobile phones and laptops near the scrotal region), and excessive heat exposure (e.g., sauna, industrial ovens).

iii. Environmental factors: exposure to pesticides, ionizing radiation, heavy metals, industrial pollutants, organic and inorganic chemicals, and xenoestrogens.

iv. Gonadotoxic medications: antidepressants, 5α-reductase inhibitors, anabolic steroids and their precursors/metabolites, antibiotics (e.g., aminoglycosides, neomycin, gentamicin, macrolides), antifungals (e.g., ketoconazole), antivirals (e.g., ribavirin), antiretrovirals, chronic opioid use, H2 histamine receptor blockers (e.g., famotidine, cimetidine), calcium channel blockers, and antigout medications (e.g., colchicine).

Men undergoing gonadotoxic therapies such as chemotherapy (e.g., alkylating agents, cisplatin, methotrexate, BEP regimen, carboplatin) and radiotherapy should be warned about the risk of temporary or permanent infertility. In such cases, semen cryopreservation or, when azoospermia is already present, testicular tissue cryopreservation should be performed before treatment initiation. Cryopreservation of spermatogonia is being investigated as a fertility preservation strategy for children and adolescents, but it is not yet standard practice (23). For patients who remain azoospermic after treatment, sperm retrieval may be considered, preferably after two years, due to the potential teratogenic effects of gonadotoxic therapies. In these cases, induction of spermatogenesis with medications before retrieval may be considered.

Pharmacological Treatment

Antibiotic Therapy: It should be considered in cases of infections of the urinary or reproductive tract, including urethritis, prostatitis, orchitis, or epididymitis. Although the impact of symptomatic or asymptomatic infections on fertility remains inconclusive, clinical studies suggest that the presence of polymorphonuclear leukocytes in semen is associated with increased oxidative stress (2, 7, 24). Excessive peroxidase-positive leukocytes (>1 million/mL) indicate inflammation but do not confirm bacterial infection. Cultures and molecular tests of urethral swabs, urine, and semen may assist in pathogen identification. A threshold of $>10^3$ colony-forming units (CFU)/mL in semen characterizes significant bacterio-

spermia. Given the variable culture positivity, collecting specimens after prostatic massage (modified Meares-Stamey test) is recommended to increase diagnostic sensitivity. Female partners should be evaluated and treated appropriately in cases of confirmed infection.

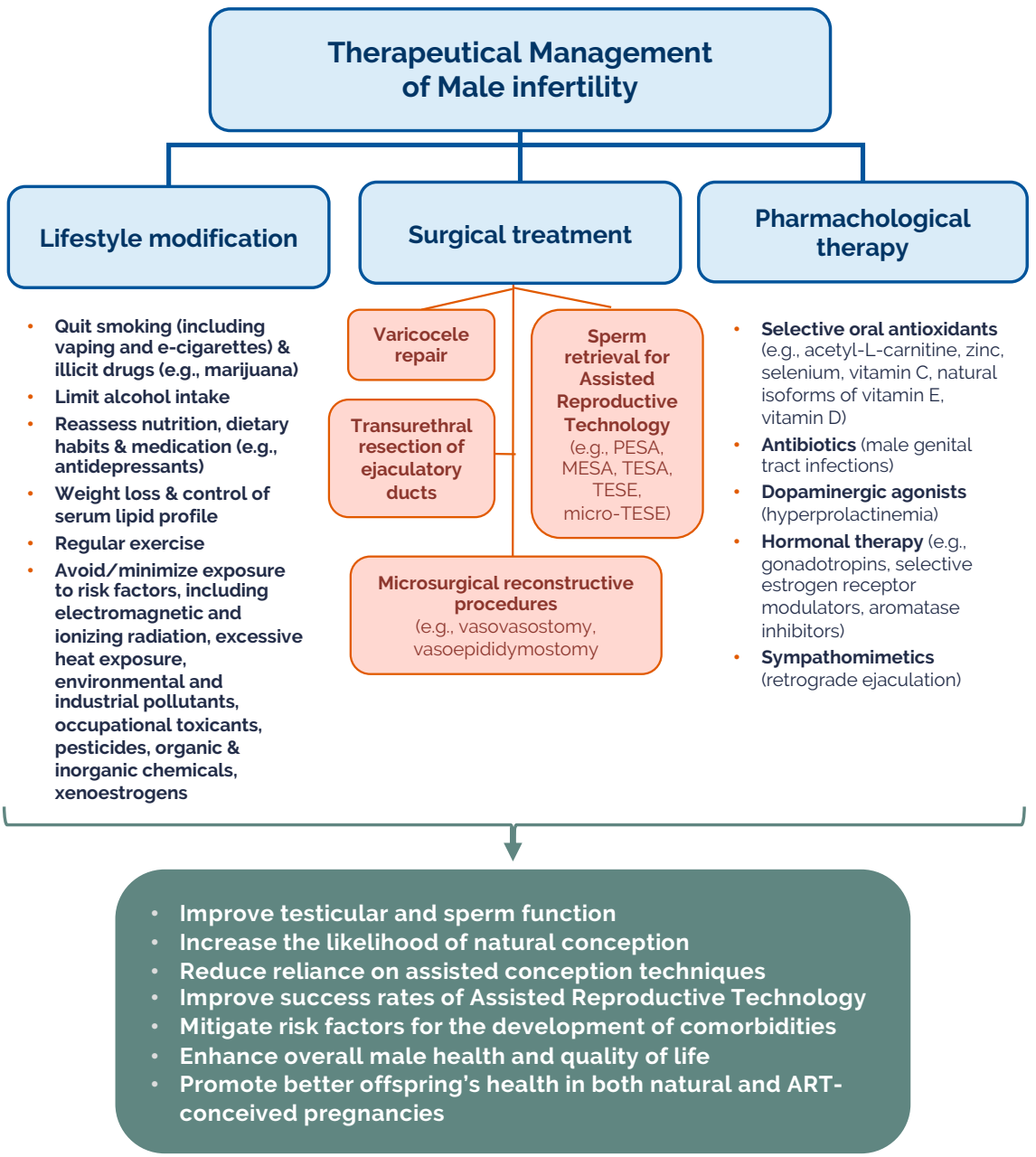
Oral Antioxidants: Selective oral antioxidants, produced from high-quality raw materials and administered at appropriate doses (e.g., acetyl-L-carnitine, zinc, selenium, vitamin C, natural isoforms of vitamin E, vitamin D), have been incorporated into the management of male infertility as adjuvant therapy (25). Studies have shown reductions in oxidative stress (OS), damage to the plasma and mitochondrial membranes, and sperm DNA fragmentation (25-29). However, the evidence remains limited and heterogeneous. Use should be individualized and maintained for at least three months (20). There is no consensus on the ideal formulation or treatment duration (1, 7, 8). Notably, over supplementation may be deleterious to semen quality (1, 7, 8, 23, 24).

Prebiotics and Probiotics Supplementation: It is under investigation but lacks robust evidence (8). Their routine use is not recommended, although they may be considered in cases requiring prolonged antibiotic treatment for genital infections.

Hormonal Therapy: Recommended for specific subgroups, summarized below (1, 2, 5, 7, 8, 30, 31).

- **Hyperprolactinemia:** Dopaminergic agonists (e.g., cabergoline, bromocriptine) help normalize prolactin levels and restore reproductive function.
- **Hypogonadotropic Hypogonadism:** Gonadotropin therapy (FSH, hCG, hMG), administered in individualized regimens, induces spermatogenesis in about 75% of men.
- **Idiopathic Oligozoospermia:** FSH administration (typically 150 IU two to three times per week for at least three to four months) may be considered in eugonadal men with baseline FSH levels between 1.5–8 mIU/mL. Meta-analyses and randomized studies show significant increases in sperm concentration and total sperm count, as well as improvements in natural and ART pregnancy rates. FSH may also improve markers such as AMH, inhibin B, and sperm DNA fragmentation. hCG alone or in combination with FSH may be used in men with biochemical hypogonadism.
- **Non-obstructive Azoospermia (NOA) with Hypogonadism:** Hormonal stimulation with hCG (alone or with FSH) may improve the likelihood of successful sperm retrieval. Although recent advances support hormonal stimulation in specific contexts, randomized clinical trials are needed before this can be recommended routinely.
- **Other Medications:**
  - Selective Estrogen Receptor Modulators (e.g., clomiphene citrate): Block estrogen receptors in the hypothalamus, increasing GnRH and consequently gonadotropin release. Meta-analyses show improvements in semen and hormonal parameters and increased pregnancy rates, though study quality is low.
  - Aromatase Inhibitors (e.g., anastrozole): Reduce peripheral conversion of testosterone to estradiol, enhancing stimulation of the hypothalamic-pituitary-gonadal axis. Though off-label, these agents improve hormonal and semen parameters with an apparent safety profile. It may be considered when the testosterone/estradiol ratio is <10 (testosterone in ng/dL and estradiol in pg/mL).
  - Sympathomimetics (e.g., pseudoephedrine): May be used in cases of retrograde ejaculation with variable efficacy.
  - Exogenous testosterone: contraindicated in men desiring fertility, as it inhibits the hypothalamic-pituitary-gonadal axis and spermatogenesis. In such cases, testosterone must be discontinued, and testicular function can be restored using hCG, FSH, selective estrogen receptor modulators, or aromatase inhibitors.

Figure 1. Therapeutic approaches to male infertility.



Management strategies include lifestyle modification, pharmacological therapy, surgical interventions, and sperm retrieval techniques for assisted reproductive technology (ART). Lifestyle changes aim to reduce modifiable risk factors such as smoking, poor diet, obesity, and environmental exposures. Pharmacological treatments involve antioxidants, antibiotics, hormonal therapies, and sympathomimetics. Surgical options include varicocele repair, microsurgical reconstructions (vasovasostomy and vasoepididymostomy), and transurethral resection of ejaculatory ducts. Sperm retrieval procedures (PESA, MESA, TESA, TESE, micro-TESE) are employed mainly for ART. These interventions collectively seek to optimize male reproductive function, enhance the chance of natural or assisted conception, and promote overall male and offspring health.

The APHRODITE criteria is a recent tool that helps identify candidates for hormonal therapy by classifying patients into clinical subgroups (e.g., hypogonadotropic hypogonadism, idiopathic infertility, NOA, unexplained infertility), thereby facilitating personalized therapeutic planning (25).

Surgical Treatment

Varicocelectomy: The surgical repair of clinical varicocele is associated with improvement in semen parameters, increased rates of natural and ART-assisted pregnancies, and reduction in oxidative stress and sperm DNA fragmentation (1-3, 7, 8, 32, 33-37). The intervention is indicated for infertile men with clinical varicocele (grades I to III with venous reflux) accompanied by semen abnormalities (concentration, motility, and/or morphology, or DNA fragmentation) or altered biochemical markers (e.g., creatine kinase, reactive oxygen species) (7, 34). The preferred surgical technique is microsurgical subinguinal varicocelectomy due to its high success rate and lower complication rate (1, 7, 8). Surgery aims to improve spermatogenesis by restoring testicular homeostasis and steroidogenesis. Approximately 70% of treated men show improvement in semen parameters, usually observed starting from the third postoperative month.

In cases of NOA, varicocelectomy may lead to the appearance of spermatozoa in the ejaculate or improve the chances of successful sperm retrieval, particularly in patients with histological findings of hypospermatogenesis or maturation arrest (38). The decision to recommend repair in NOA males should consider the couple's clinical context, given that most supporting data comes from observational studies (1, 7, 8).

Obstructive Azoospermia (OA): Management depends on the underlying etiology, site of obstruction, clinical context, and patient preferences (3, 7, 8, 38). Men with previous vasectomy benefit from microsurgical reversal (vasovasostomy or vasoepididymostomy), with high patency rates when performed by experienced microsurgeons (3). Selected cases of inflammatory or congenital obstruction (e.g., unilateral congenital absence of the vas deferens with segmental blockage) may also be eligible for reconstructive surgery. In contrast, intratesticular obstructions usually require surgical sperm retrieval for ART.

Reconstructive procedures may be combined with sperm collection and cryopreservation for future ART use. Ejaculatory duct obstruction, whether due to inflammation or cysts, may be treated with transurethral resection or vesiculoscopy to restore semen flow (39).

Surgical Sperm Retrieval for ART

Obstructive Azoospermia: In OA, sperm retrieval can usually be achieved using percutaneous epididymal aspiration (PESA), testicular aspiration (TESA), microsurgical epididymal aspiration (MESA), or testicular sperm extraction (TESE) (3, 7, 8, 11, 38). Each method has pros and cons regarding sperm yield and quality and the feasibility of cryopreservation for future ICSI cycles. ICSI outcomes using epididymal or testicular sperm, whether fresh or frozen, are similar, provided the laboratory is experienced.

Non-obstructive Azoospermia: In NOA men with primary spermatogenic failure, focal areas of sperm production may exist, with retrieval success rates around 50%, depending on the technique and patient population (3, 7, 8, 11). Retrieved sperm should be used for ICSI, which can result in healthy offspring (11). Microdissection TESE (micro-TESE) is the gold standard due to its superiores efficacy and reduced tissue removal compared to conventional TESE, thereby minimizing testicular damage (3, 7, 8, 40). Studies show micro-TESE is about 1.5 times more effective than conventional TESE, with lower complication rates and proven success even after failed TESA or conventional TESE (3, 7, 8, 40).

Fine-needle aspiration mapping has been proposed to guide TESE prognosis. However, it requires two separate procedures (diagnostic and therapeutic) and lacks randomized trials or cost-effectiveness studies to justify routine use (7).

Factors influencing sperm retrieval success include testicular histology, hormone levels (FSH, inhibin B, AMH, testosterone), presence of varicocele, and Y chromosome microdeletions (40-42). Histological findings of hypospermatogenesis are associated with higher retrieval rates, whereas the Sertoli cell-only pattern is a poor prognostic factor. Better outcomes are observed in men with lower FSH and AMH levels and higher in-

hibin B and testosterone levels (41, 42). Clinical varicocele is a negative prognostic factor, whereas its repair is beneficial. (3, 33, 41, 42). Hormonal stimulation before retrieval may improve outcomes, although evidence is mostly from retrospective studies (7, 8, 42, 43). Complete deletions of AZFa or AZFb regions of the Y chromosome contraindicate sperm retrieval, while men with AZFc deletions have a ~50% chance of success (7, 8, 40).

Non-azoospermic men: Testicular sperm (via TESA, TESE, or micro-TESE) may be used for ICSI in non-azoospermic men with high sperm DNA fragmentation when other corrective measures (e.g., varicocelectomy, lifestyle modification, withdrawal of gonadotoxins, antioxidant therapy, treatment of hormonal imbalances), if applicable, have failed (8, 44). Testicular sperm generally have lower DNA fragmentation compared to ejaculated sperm, and emerging data suggest improved ICSI outcomes in these cases (44). The decision must be shared with the couple.

Assisted Reproduction Techniques

While ART may overcome male infertility, evaluating the male partner remains critical to identifying medically relevant conditions, providing counseling on long-term health, and directing appropriate therapy (1, 2, 10, 11). Several causes of male infertility are amenable to medical or surgical correction. Addressing treatable male factors may enhance ART success and improve offspring health (2, 10).

Conversely, indiscriminate use of ART for male factor infertility is not recommended due to potential risks such as ovarian hyperstimulation syndrome and multiple pregnancies. Furthermore, ICSI-conceived children may have higher neonatal morbidity, obstetric complications, and congenital anomalies compared to those conceived naturally (11, 45). Epigenetic alterations and impaired neurodevelopment have also been observed more frequently (11, 46). Therefore, the judicious use of ART in male infertility is essential, in alignment with evidence-based and personalized reproductive care. A call for the responsible use of ICSI is critically important to safeguard the fertility and overall health of future generations (47).

CONCLUSIONS

In at least 50% of infertile couples, a male factor is identified as a primary or contributing cause. Therefore, every infertile couple should have their male partner comprehensively evaluated. In specific cases, a multidisciplinary approach involving a nutritionist, geneticist, endocrinologist, and psychologist may be necessary to ensure comprehensive and personalized management. Interventions such as lifestyle modification, antioxidant therapy, varicocelectomy, and hormonal treatment aim to restore testicular function, improve general health, and increase the likelihood of natural and ART-assisted conception while promoting physical and metabolic well-being. All therapeutic strategies should be maintained for at least one complete spermatogenic cycle (approximately three months), with ongoing clinical and laboratory monitoring. Proper guidance, rational use of diagnostic and therapeutic resources, and active patient and partner participation are essential for optimizing outcomes and achieving biological parenthood.

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CONFLICT OF INTEREST

None declared.

REFERENCES

1. Eisenberg ML, Esteves SC, Lamb DJ, Hotaling JM, Giwercman A, Hwang K, et al. Male infertility. Nat Rev Dis Primers. 2023;9(1):49. doi: 10.1038/s41572-023-00759-x.

2. Esteves SC. Who cares about oligozoospermia when we have ICSI. Reprod Biomed Online. 2022;44:769-75. doi: 10.1016/j.rbmo.2022.04.012.
3. Esteves SC, Miyaoka R, Agarwal A. Surgical treatment of male infertility in the era of intracytoplasmic sperm injection - new insights. Clinics (Sao Paulo). 2011;66:1463-78. doi: 10.6061/clinics/2011(08)02.
4. Fraga LG, Gismondi JP, Sanvido LV, Lozano AFQ, Teixeira TA, Hallak J. Clinical and laboratorial evaluation of male infertility. A Detailed Practical Approach. Arch Med Res. 2024;55:103139. doi: 10.1016/j.arcmed.2024.103139.
5. Esteves SC, Santi D, Simoni M. An update on clinical and surgical interventions to reduce sperm DNA fragmentation in infertile men. Andrology. 2020;8:53-81. doi: 10.1111/andr.12624.
6. Esteves SC, Miyaoka R, Agarwal A. An update on the clinical assessment of the infertile male. [corrected]. Clinics (Sao Paulo). 2011;66:691-700. doi: 10.6061/clinics/2011(04)11.
7. Minhas S, Boeri L, Capogrosso P, Cocci A, Corona G, Dinkelman-Smit M, et al. European Association of Urology Guidelines on Male Sexual and Reproductive Health: 2025 Update on Male Infertility. Eur Urol. 2025:S0302-2838(25)00148-4. doi: 10.1016/j.eururo.2025.03.017.
8. Brannigan RE, Hermanson L, Kaczmarek J, Kim SK, Kirkby E, Tanrikut C. Updates to Male Infertility: AUA/ASRM Guideline (2024). J Urol. 2024;212:789-99. doi: 10.1097/JU.0000000000004479.
9. Esteves SC. Evolution of the World Health Organization semen analysis manual: where are we? Nat Rev Urol. 2022;19:439-46. doi: 10.1038/s41585-022-00589-x.
10. Esteves SC, Humaidan P. Towards infertility care on equal terms: a prime time for male infertility. Reprod Biomed Online. 2023;47:11-4. doi: 10.1016/j.rbmo.2023.03.009.
11. Esteves SC, Roque M, Bedoschi G, Haahr T, Humaidan P. Intracytoplasmic sperm injection for male infertility and consequences for offspring. Nat Rev Urol. 2018;15:535-62. doi: 10.1038/s41585-018-0067-1.
12. Teixeira T, Nazima M, Hallak J. Male sexual quality of life is maintained satisfactorily throughout life in the Amazon rainforest. Sex Med. 2018;6:90-6. doi: 10.1016/j.esxm.2018.03.002.
13. Teixeira TA, Iori I, Andrade G, Saldiva PHN, Drevet JR, Costa EMF, et al. Marijuana is associated with a hormonal imbalance among several habits related to male infertility: A retrospective study. Front Reprod Health. 2022;4:1-10. doi: 10.3389/frph.2022.1054069.
14. Hallak J, Teixeira TA, de Souza GL. Effect of Exogenous Medications and Anabolic Steroids on Male Reproductive and Sexual Health. In: Parekattil, S., Esteves S., Agarwal A. (eds) Male Infertility. Springer, Cham, 2020. doi: 10.1007/978-3-030-24655-1_13.
15. Azevedo RA, Gualano B, Teixeira TA, Nascimento BCG, Hallak J. Abusive use of anabolic androgenic steroids, male sexual dysfunction and infertility: an updated review. Front Toxicol. 2024;6:1379272. doi: 10.3389/ftox.2024.1379272.
16. Humaidan P, Haahr T, Povlsen BB, Kofod L, Laursen RJ, Alsbjerg B, et al. The combined effect of lifestyle intervention and antioxidant therapy on sperm DNA fragmentation and seminal oxidative stress in IVF patients: a pilot study. Int Braz J Urol. 2022;48:131-56. doi: 10.1590/S1677-5538.IBJU.2021.0311.
17. Behdarvandian P, Nasr-Esfahani A, Tavalaee M, Pashaei K, Naderi N, Darmishonnejad Z, et al. Sperm chromatin structure assay (SCSA®) and flow cytometry assisted TUNEL assay provide a concordant assessment of sperm DNA fragmentation as a function of age in a large cohort of approximately 10,000 patients. Basic Clin Androl. 2023;33:33. doi: 10.1186/s12610-023-00157-0.
18. Cocuzza MAS, Athayde KS, Agarwal A, Sharma RK, Pagani RL, Lucon AM, et al. Age-related increase of reactive oxygen species in neat semen in healthy fertile men. Urology (Ridgewood, N.J.). 2008;71:490-4. doi: 10.1016/j.urology.2007.10.051.
19. Soares PM, Borba EF, Bonfa E, Hallak J, Corrêa AL, Silva CA. Gonad evaluation in male systemic lupus erythematosus. Arthritis Rheum. 2007;56:2352-61. doi: 10.1002/art.22785.
20. Hallak J, Teixeira TA, Bernardes FS, Carneiro F, Duarte SAS, Pariz JR, et al. SARS-CoV-2 and its relationship with the genitourinary tract: Implications for male reproductive health in the context of COVID-19 pandemic. Andrology. 2021;9:73-9. doi: 10.1111/andr.12812.
21. Teixeira TA, Oliveira YC, Bernardes FS, Kallas EG, Duarte-Neto AN, Esteves SC, et al. Viral infections and implications for male reproductive health. Asian J Androl. 2021;23:335-47. doi: 10.4103/aja.aja_116_21.
22. Hallak J, Caldini EG, Teixeira TA, Correa MCM, Duarte-Neto AN, Zambrano F, et al. Transmission electron microscopy reveals the presence of SARS-CoV-2 in human spermatozoa associated with an ETosis-like response. Andrology. 2024;12:1799–807. doi: 10.1111/andr.13394.

23. von Rohden E, Jensen CFS, Andersen CY, Sønksen J, Fedder J, Thorup J, et al. Male fertility restoration: in vivo and in vitro stem cell-based strategies using cryopreserved testis tissue: a scoping review. Fertil Steril. 2024;122:828-43. doi: 10.1016/j.fertnstert.2024.07.011.
24. Reich MC, Heide N, Humaidan PC, Esteves SC. Asymptomatic Leukocytospermia and Assisted Reproductive Technology Outcomes: Reason for concern? Int Braz J Urol. 2025;51:e20250166. doi: 10.1590/S1677-5538.IBJU.2025.0166.
25. Moazamian A, Hug E, Villeneuve P, Bravard S, Geurtsen R, Hallak J, et al. The dual nature of micronutrients on fertility: too much of a good thing? F&S Science. 2025, ahead of print. doi: 10.1016/j.xfss.2025.02.004.
26. Drevet JR, Hallak J, Nasr-Esfahani MH, Aitken RJ. Reactive Oxygen species and their consequences on the structure and function of mammalian spermatozoa. Antioxid Redox Signal. 2022;37(7-9):481-500. doi: 10.1089/ars.2022.9574.
27. Hallak J, Teixeira TA. Oxidative Stress & Male Infertility - A necessary and conflicted indissociable marriage: How and when to call for evaluation? Int Braz J Urol. 2021;47:686-9. doi: 10.1590/S1677-5538.IBJU.2021.0339.
28. Ciccone IM, Costa EM, Pariz JR, Teixeira TA, Drevet JR, Gharagozloo P, et al. Serum vitamin D content is associated with semen parameters and serum testosterone levels in men. Asian J Androl. 2021;23:52-8. doi: 10.4103/aja.aja_117_21.
29. Andrade G, Iori I, Hsieh MK, Milani G, Zandoná PCE, Teixeira TA, et al. Serum lipid profile levels and semen quality: new insights and clinical perspectives for male infertility and men's health. Int Urol Nephrol. 2023;55:2397-404. doi: 10.1007/s11255-023-03049-w.
30. Esteves SC, Achermann APP, Simoni M, Santi D, Casarini L. Male infertility and gonadotropin treatment: What can we learn from real-world data? Best Pract Res Clin Obstet Gynaecol. 2023;86:102310. doi: 10.1016/j.bpobgyn.2023.102310.
31. Esteves SC, Humaidan P, Ubaldi FM, Alviggi C, Antonio L, Barratt CLR, et al. APHRODITE criteria: addressing male patients with hypogonadism and/or infertility owing to altered idiopathic testicular function. Reprod Biomed Online. 2024;48:103647. doi: 10.1016/j.rbmo.2024.01.023.
32. Esteves SC, Miyaoka R, Roque M, Agarwal A. Outcome of varicocele repair in men with nonobstructive azoospermia: systematic review and meta-analysis. Asian J Androl. 2016;18:246-53. doi: 10.4103/1008-682X.169562.
33. Pasqualotto FF, Sobreiro BP, Hallak J, Pasqualotto EB, Lucon AM. Induction of spermatogenesis in azoospermic men after varicocelectomy repair: an update. Fertil Steril. 2006;85:635-9. doi:10.1016/j.fertnstert.2005.08.038.
34. Sidhu RS, Hallak J, Sharma RK, Thomas AJ Jr, Agarwal A. Relationship between creatine kinase levels and clinical diagnosis of infertility. J Assist Reprod Genet. 1998;15:188-92. doi:10.1023/A:1022578823493.
35. Esteves SC, Zini A, Coward RM, Evenson DP, Gosálvez J, Lewis SEM, et al. Sperm DNA fragmentation testing: Summary evidence and clinical practice recommendations. Andrologia. 2021;53:e13874. doi:10.1111/and.13874.
36. Lira FT Neto, Campos LR, Roque M, Esteves SC. From pathophysiology to practice: addressing oxidative stress and sperm DNA fragmentation in varicocele-affected subfertile men. Int Braz J Urol. 2024;50:530-60. doi:10.1590/S1677-5538.IBJU.2023.0422.
37. Lira Neto FT, Roque M, Esteves SC. Effect of varicocelectomy on sperm deoxyribonucleic acid fragmentation rates in infertile men with clinical varicocele: a systematic review and meta-analysis. Fertil Steril. 2021;116:696-712. doi:10.1016/j.fertnstert.2021.05.134.
38. Miyaoka R, Esteves SC. Predictive factors for sperm retrieval and sperm injection outcomes in obstructive azoospermia: do etiology, retrieval techniques and gamete source play a role? Clinics (Sao Paulo). 2013;68(Suppl 1):111-9. doi:10.6061/clinics/2013(Sup01)13.
39. Achermann APP, Esteves SC. Diagnosis and management of infertility due to ejaculatory duct obstruction: summary evidence. Int Braz J Urol. 2021;47:868-81. doi:10.1590/S1677-5538.IBJU.2020.0911.
40. Achermann APP, Pereira TA, Esteves SC. Microdissection testicular sperm extraction (micro-TESE) in men with infertility due to nonobstructive azoospermia: summary of current literature. Int Urol Nephrol. 2021;53:2193-210. doi:10.1007/s11255-021-02913-3.

41. Arshad MA, Majzoub A, Esteves SC. Predictors of surgical sperm retrieval in non-obstructive azoospermia: summary of current literature. Int Urol Nephrol. 2020;52:2015-38. doi:10.1007/s11255-020-02585-3.
42. Esteves SC, Achermann APP, Miyaoka R, Verza S Jr, Fregonesi A, Riccetto CLZ. Clinical factors impacting microdissection testicular sperm extraction success in hypogonadal men with nonobstructive azoospermia. Fertil Steril. 2024;122:636-47. doi:10.1016/j.fertnstert.2024.06.012.
43. Tharakan T, Corona G, Foran D, Salonia A, Sofikitis N, Giwercman A, et al. Does hormonal therapy improve sperm retrieval rates in men with non-obstructive azoospermia: a systematic review and meta-analysis. Hum Reprod Update. 2022;28:609-28. doi:10.1093/humupd/dmac016.
44. Esteves SC, Coimbra I, Hallak J. Surgically retrieved spermatozoa for ICSI cycles in non-azoospermic males with high sperm DNA fragmentation in semen. Andrology. 2023;11:1613-34. doi:10.1111/andr.13279.
45. Majzoub A, Viana MC, Achermann APP, Ferreira IT, Laursen RJ, Humaidan P, et al. Non-Obstructive Azoospermia and Intracytoplasmic Sperm Injection: Unveiling the Chances of Success and Possible Consequences for Offspring. J Clin Med. 2024;13:4939. doi:10.3390/jcm13164939.
46. Sciorio R, Tramontano L, Rapalini E, Bellaminutti S, Bulletti FM, D'Amato A, et al. Risk of genetic and epigenetic alteration in children conceived following ART: Is it time to return to nature whenever possible? Clin Genet. 2023;103:133-45. doi:10.1111/cge.14334.
47. Hallak J. A call for more responsible use of Assisted Reproductive Technologies (ARTs) in male infertility: the hidden consequences of abuse, lack of andrological investigation and inaction. Transl Androl Urol. 2017;6:997-1004. doi:10.21037/tau.2017.08.06.

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