EUROPEAN ACADEMY OF ANDROLOGY

Literature alert

May 2026

The May edition of the EAA literature alert brings you a selection of noteworthy publications in all areas of andrology. The EAA Centre in L'Aquila is showcased in this issue with two articles in our journal *Andrology*.

Keywords: paternal age and reproductive outcomes, spinal cord injury and testosterone, gonadotrophins, testicular cancer, epididymo-orchitis, testis damage in COVID-19, lipid levels and semen quality, headache and steroid hormone dysfunction, sperm vacuolisation, effects of exposure to organochlorine compounds in humans and PFAS in mice, genetics of PCOS/PMOS, epididymal extracellular vesicles, in vitro maturation of Sertoli cells, semen-derived exosomes as drug vehicles. There is also a new edition of a book on genetic and epigenetic damage in human spermatozoa. If you wish to share a good publication with EAA members – send a note to *RajpertDeMeyts.EAA@gmail.com*.

Clinical andrology and epidemiology

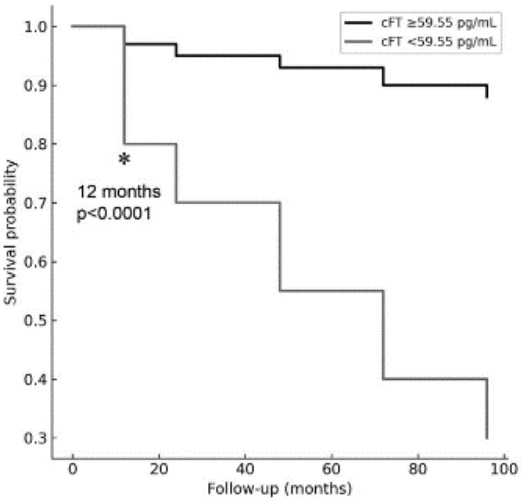
ANDROLOGY

Several ART clinics in Italy, including the EAA Centre in L'Aquila, evaluated jointly the association between paternal age and live birth outcomes in couples undergoing IVF or ICSI.

Among the 6262 couples assessed, 42.8% involved normospermic men. Advancing paternal age was associated with a reduced probability of live birth in ART, even among normospermic men and after accounting for maternal age.

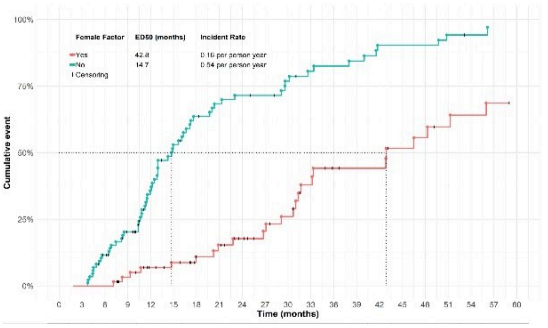
Maruccia S, Terzoni S, Tienforti D, Renzini MM, Bartoli E, Vitali M, Kinzikeeva E, Maragno L, Brigante C, Ricci C, Cassani A, Bozzini G, Guglielmo MC, Barbonetti A, Canto MD. Advanced Paternal Age Reduces Live Birth Rates in Normosper-mic Men Undergoing ART: A Large Retrospective Cohort Study. ***Andrology***. 2026 May 14. https://doi.org/10.1111/andr.7025

The EAA Andrology Centre in L'Aquila conducted a retrospective cohort study of baseline calculated free testosterone (cFT) in 152 patients with chronic spinal cord injury (SCI). The study found that low cFT independently predicted all-cause mortality in men with chronic SCI, suggesting that cFT may represent a biomarker of systemic frailty in this high-risk population.



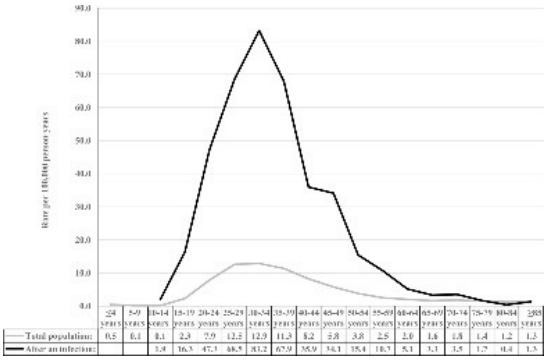
Tienforti D, Spagnolo L, Moretto C, Terrana G, Geronimo RD, Perfetto E, Felzani G, Baroni MG, Barbonetti A. Low Free Testosterone Is Independently Associated with Long-Term Mortality in Men with Chronic Spinal Cord Injury. ***Andrology***. 2026 May 1. https://doi.org/10.1111/andr.70251

This study from Australia evaluated determinants of fertility outcomes in men with pathologic gonadotropin-deficiency undergoing hCG/FSH treatment. Most men in this cohort achieved sperm output and fertility within a year, with the greatest impact on fertility outcomes being detrimental female fertility factors.



Gialouris JV, Conway AJ, Idan A, Savkovic S, Hermosilla R, Muir CA, Bacha F, Zhang T, Hou W, Jayadev V, Handelsman DJ. Efficacy of Gonadotropin Therapy to Induce Spermatogenesis and Fertility in Men with Pathologic Gonadotropin Deficiency. ***J Clin Endocrinol Metab***. 2026 Apr 22;111(5):1450-1458. https://doi.org/10.1210/clinem/dgaf588

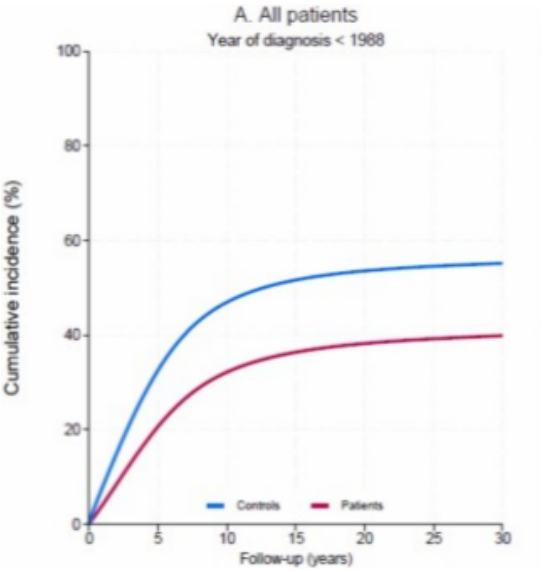
This nationwide Swedish study (> 8 million men) analysed incidence rates of testicular cancer (TC) in relation to prior epididymo-orchitis (EO) or urinary tract infections (UTI). In the study period the TC incidence rate rose from 2.8 (1964–73) to 8.4 (2014–18). The associations between TC and EO (but not UTI) were strong (SIR: 6.3), particularly for TC diagnosed in the same year as EO (SIR: 85) and persisted for several years. Clinicians should keep a heightened awareness of TC in patients with epididymo-orchitis.



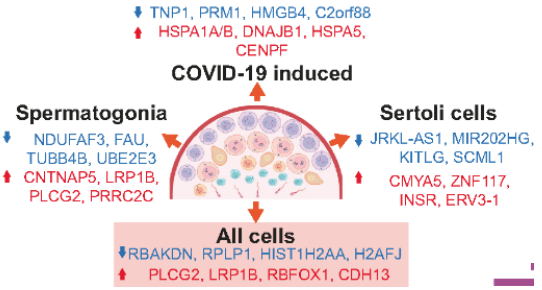
Jansåker F, Li X, Sundquist K. Testicular cancer incidence and associations with prior epididymo-orchitis or urinary tract infections: a national cohort study in Sweden, 1964–2018. ***BMJ Oncology***. 2026; 5:e001078. https://doi.org/10.1136/bmjonc-2026-001078

This study from Norway assessed post-diagnosis paternity in testicular cancer (TC) survivors and age-matched controls. The TC survivors have generally favourable probability of post-TC fatherhood at least once, but the probability is slightly lower than in the controls. Pre-diagnosis childlessness reduces post-TC paternity.

Fosså SD, Myklebust TÅ, Brydøy M, Negaard HFS, Klepp OH, Dahl AA, Stangenes KM, Kleveland CR, Seljeflot EB, Haugnes HS. Post-treatment paternity in testicular cancer survivors: Do demographic variables matter? ***Cancer Epidemiol***. 2026 Jun; 102:103074. https://doi.org/10.1016/j.canep.2026.103074

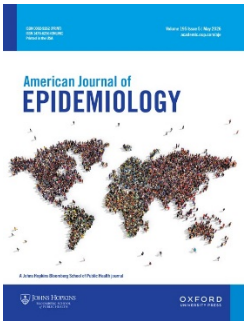


This comprehensive study analysed testis tissue samples and reproductive outcomes in COVID-19 patients in comparison to controls. The findings demonstrated that SARS-CoV-2 can disrupts spermatogenesis with persistently reduced numbers of Sertoli-cells and spermatogonia, alter transcriptional landscape (with a new COVID-19-specific cluster), and have long-term consequences for male fertility.



Brieno-Enriquez M; *et al. et* Orwig K, Elemento O, Marquez C, Ghosh S, Bassas L, Costa G, Roig I. SARS-CoV-2 infection reduces the number of spermatogonial stem cells and dysregulates the transcriptional landscape of the human testis. ***Res Sq*** [**Preprint -not peer reviewed**]. 2026 Apr 21:rs.3.rs-9371895. https://doi.org/10.21203/rs.3.rs-9371895/v1

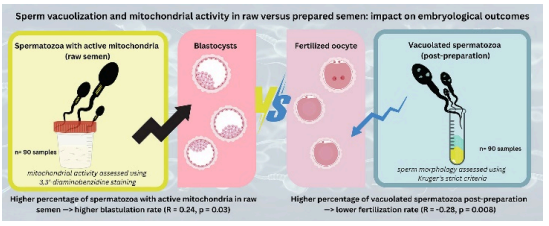
The associations between elevated lipid levels and semen parameters were examined in 2321 men from couples with fertility problems, using data from the Folic Acid and Zinc Supplementation Trial (FAZST). Men with elevated lipid levels (58% of the cohort) had reduced semen volume and altered morphology, some also reduced sperm count and total motility.



Grandi SM, Mumford SL, Hinkle SN, Tailor LS, Sjaarda LA, Flanagan KS, Aston KI, Jenkins T, Hotaling J, Johnstone EB, Van Voorhis BJ, Ryan G, Perkins NJ, Schisterman EF. Elevated lipid levels and altered semen parameters in men of couples seeking fertility care. ***Am J Epidemiol***. 2026 May 12: kwag103. https://doi.org/10.1093/aje/kwag103

Men with cluster headache (CH) often present with a state of compensated hypogonadism. This study identified distinct adrenal steroid hormone profiles in episodic and chronic CH. FreeT/LH ratio was reduced by 35% in patients with CH after adjusting for age, sleep duration, and use of acute medication. A shared genetic risk allele, rs112572874 between free T and cluster headache was identified.

Westgate CSJ, Lylloff T, Kristensen DM, *et al et* Juul A, Jensen RH, Petersen AS. Adrenal gland dysfunction in males with cluster headache. ***J Headache and Pain*** 2026, https://doi.org/10.1186/s10194-026-02386-z



This multicentre prospective study of couples undergoing ICSI demonstrated that in prepared semen, vacuolated sperm percentage may predict fertilization rate, whereas the percentage of spermatozoa with active mitochondria in raw semen may predict blastulation rate.

Raad G, Sayegh JE, Roz NE, Bazzi M, Yarkiner Z, Serdarogullari M, Liperis G, Ammar O, Fakih F, Mourad Y, Fakih C. Sperm vacuolization and mitochondrial activity in raw versus prepared semen: effect on embryological outcomes. ***Reprod Biomed Online***. 2026 May;52(5):105262. https://doi.org/10.1016/j.rbmo.2025.105262

Developmental exposure to organochlorine compounds, including polychlorinated compounds (PCBs), and perfluorinated compounds (PFASs) was associated with sperm aneuploidy in young adulthood. Higher concentrations of organochlorines in cord blood and in serum at ages 7, 14 and 22 years were associated with increased proportions of chromosomal disomies in sperm, suggestive of adverse effects on the formation of male germ cells.

Perry MJ, Meddis A, Young HA, Robbins CR, Budtz-Jørgensen E, Jørgensen N, Halling J, Weihe P, Grandjean P, Petersen MS. In utero and childhood exposure to organochlorines and perfluorinated chemicals in relation to sperm aneuploidy in adulthood. ***Environ Health***. 2026 May 2. https://doi.org/10.1186/s12940-026-01303-w

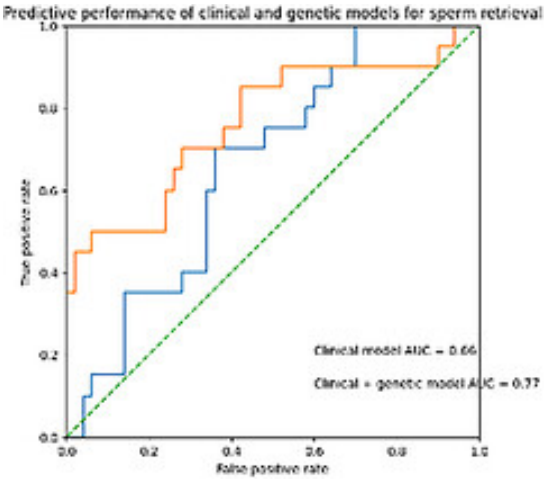
Androgenetics

The genetic landscape of polycystic ovary syndrome (PCOS), which was recently renamed to **polyendocrine metabolic ovarian syndrome (PMOS),** was comprehensively reevaluated. The study expanded the number of PCOS/PMOS genome-wide significant loci to 29 (incl. *FTO, SHBG*, *FSHB, FSHR*, *CYP3, ERBB3 /4, ZBTB16, INHBB*, *AMH* and *TEX41)* and identified 31 associated plasma proteins. The identified loci underscore the sex hormonal origins of the disorder, also of relevance for andrologists. A polygenic risk score was associated with adverse cardiometabolic outcomes, with differing relevance of testosterone and BMI in women and men.

In men, there is a corresponding increase in higher free androgen index that explains the connection between PCOS variants and male-pattern balding.

Moolhuijsen LME *et al. et* Genes and Health Research Team; DBDS Genomic Consortium; 23andMe Research Team; *et al. et*, Ong KK, Goodarzi MO, Davis LK, Dunaif A, Lindgren CM, Laven JSE, Franks S, Visser JA, Welt CK, Karaderi T, Day FR. Genomic analyses implicate hormonal and metabolic dysregulation in polycystic ovary syndrome. ***Nat Genet***. 2026 May;58(5):1040-1050. doi: 10.1038/s41588-026-02543-9. https://doi.org/10.1038/s41588-026-02543-9

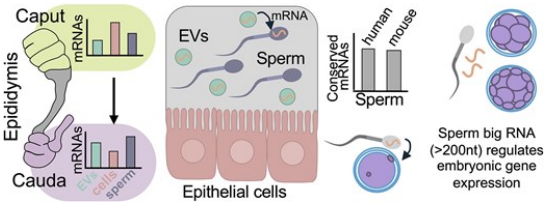
A retrospective cohort of patients with Klinefelter syndrome was assessed for possible associations between *FSHB* and *FSHR* polymorphisms and hormonal parameters, and sperm retrieval rate. The contribution of the variants was only incremental but additive genetic modelling showed a potential allele-dose effect of *FSHR* c.29 G > A on reproductive outcomes.



Graziani A, Grande G, Rocca MS, Iafrate M, Selice R, Di Mambro A, Ferlin A. “Impact of FSHB and FSHR Genes Polymorphisms on Hormonal Profile and Sperm Retrieval Outcome in Men with Klinefelter

Syndrome: A Clinical–Genetic Predictive Study." ***Andrology*** (2026): 19 May. https://doi.org/10.1111/andr.70262

Translational and basic andrology



A comprehensive analysis of messenger RNAs (mRNA) of mouse sperm and epididymal epithelium, revealed that sperm picks up mRNAs from the epididymal extracellular vesicles (EVs). The study also revealed that some mRNAs can drive gene regulation when microinjected into zygotes.

These findings suggest that sperm, including human, can influence preimplantation embryo gene expression not only via small RNAs but also larger RNA species.

Trigg NA, Lee GS, Leach AG, Conine CC. Epididymal extracellular vesicles harbor and convey mRNA to sperm for transfer to zygotes, ***Nucleic Acids Research*****,** 54 (7), 24 April 2026, gkag330, https://doi.org/10.1093/nar/gkag330

This work investigated Sertoli cell maturation and functionality after in vitro maturation of frozen-thawed mouse prepubertal testis tissue for up to 30 days. The expression of Sertoli cell markers was similar between the cultured explants and control tissues, and the explants secreted inhibin B.

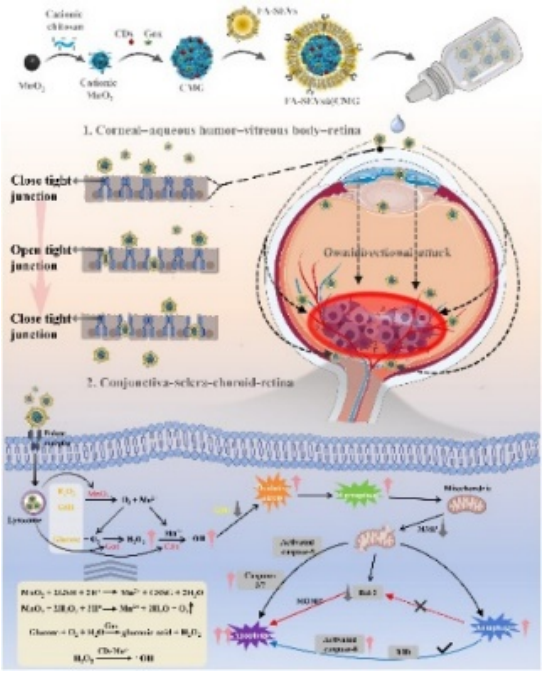
However, there was no progression into spermatogenesis, even after supplementation with FSH.

Moutard L, Dufour M, Rives N, Basille-Dugay M, Chemin E, Rousseau V, Feraille A, Rondanino C, Dumont L (2026) Maturation-associated changes in Sertoli cells following in vitro culture of frozen-thawed prepubertal mouse testicular tissue. ***Front. Reprod. Health*** 8:1835316. https://doi.org/10.3389/frph.2026.1835316

A multigenerational PFAS exposure regimen in mice was used to emulate a real-life human PFAS exposure. Testicular accumulation of PFAS was correlated with alterations in sperm production. PFAS-exposure did not compromise overall fertility but did alter the sperm epigenome. The effects differed across generations and were most pronounced at F1, in which the pups were larger.

Gillespie L, Martin JH, *et al. et* Nixon B. Multigenerational exposure to per- and polyfluoroalkyl substances (PFAS) negatively impacts the reproductive health of male mice. ***Environ Res***. 2026 Apr 20;301:124528. https://doi.org/10.1016/j.envres.2026.124528

Do you know that semen-derived exosomes (SEVs) can penetrate ocular barriers? SEVs express EGF, which mediates reversible tight-junction disruption. Eye drops that contain drug-carrying SEVs from pig semen can inhibit growth of retinal cancer in mice without affecting vision. Researchers hope that the drops could be developed into a treatment for children with retinoblastoma.



Zhao J, *et al. et,* Zhang Y. Harnessing semen-derived exosomes for noninvasive fundus drug delivery: A paradigm for exosome-based ocular fundus therapeutics. ***Sci Adv.*** 2026 Mar 27;12(13):eadw7275. https://doi.org/10.1126/sciadv.adw7275

Andrology lab

A methodology study with self-explanatory title:

Jensen MB, Povlsen BB, Heide N, Lykkegaard J, Mulato MG, Sousa S, Humaidan P, Esteves SC. SwimCount Harvester™ versus Density Gradient Centrifugation: A Pilot Study exploring Sperm DNA Fragmentation and Motile Sperm Recovery. ***Int Braz J Urol***. 2026 Sep-Oct;52(5):e20260327. DOI: 10.1590/S1677-5538.IBJU.2026.0327

Book of the Month

Genetic and Epigenetic Damage in Human Spermatozoa
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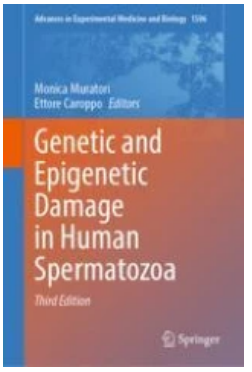
Editors: Monica Muratori and Ettore Caroppo
New edition presents a thorough update of the state of science for genetic damage in human spermatozoa. The editors and several authors are EAA members
The book contains 10 chapters and discusses the latest findings from the field of epigenetics, including methods to investigate sperm epigenome and miRNA
https://link.springer.com/book/10.1007/978-3-032-18376-7#toc



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