



Literature alert

August 2026

The peak summer holiday time in the Northern hemisphere has ended, and you are now ready to return to work with renewed energy. I urge you to read the entire latest issue of *Andrology*, which – in addition to interesting regular articles – contains several pertinent commentaries which are normally not highlighted in our alerts. Other journals also published a lot of noteworthy articles across the clinical, translational and basic science spectrum of andrology. Enjoy the reading!

The latest issue of *Andrology*

The September 2026 issue (released in early August) contains several editorials, reviews and commentaries on **currently debated issues**, including:



- The (mis)use of antioxidants and 'nutraceuticals' in male infertility (doi.org/10.1111/andr.70279)
- Limiting (or not?) of the number of offspring per sperm donor (*in the aftermath of the recent multiple transmission of a pathogenic TP53 variant from a donor*) (doi.org/10.1111/andr.70219, doi.org/10.1111/andr.70308)
- Management of cryptorchidism in post-pubertal/adult patients (doi.org/10.1111/andr.70311)
- Preoperative testicular volume (doi.org/10.1111/andr.70223)
- Nomograms for mTESE in NOA (doi.org/10.1111/andr.70174)

The issue contains many interesting studies, some previously highlighted in our alerts. The **Editor's picks** are:

- **Clinical:** Bier S *et al.* Healthy Aging Men Do Not Suffer from Relevant Limitations of Their Reproductive Functions. doi.org/10.1111/andr.70147
- **Basic:** Fan XJ *et al.* Proteomic Profiling of Cryopreservation-Induced Alterations in Rhesus Macaque Sperm.
- doi.org/10.1111/andr.70303

The contents of the September issue: onlinelibrary.wiley.com/toc/20472927/2026/14/6

Also released in August was the special issue with the programme and abstracts of the 51st ASA Annual Meeting (18-21 April 2026, Scottsdale, Arizona):

onlinelibrary.wiley.com/toc/20472927/2026/14/S1?campaign=woletoc

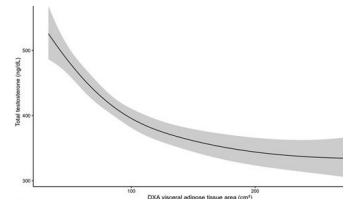
Clinical andrology and epidemiology

Among men in the first year after stopping androgen abuse, psychological symptoms and reduced quality-of-life were stronger associated with psychiatric comorbidity than biochemical recovery. These findings challenge the assumption that androgen withdrawal symptoms are predominantly driven by hypogonadism and supports developing psychological and behavioural interventions.

Grant B, Kean J, de Silva NL, Aguilera R, Quinton OCB, Gumssani M, Bassett P, Dhillo WS, Lingford-Hughes A, Wolff K, Jayasena CN. Clinical features of androgen abuse withdrawal in men during the first year of cessation: a community dwelling study. *J Clin Endocrinol Metab.* 2026 Aug 13;111(9):2649-2663. doi.org/10.1210/clinem/dgag110

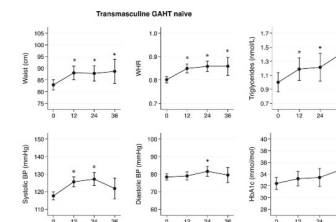


A cross-sectional NHANES-based analysis of 4948 US men (20-59 y.), demonstrated that among obesity-related parameters, visceral adiposity, rather than BMI or waist circumference, best correlated with low testosterone. In addition, testosterone deficiency in some men appears to be a phenotype of visceral fat biology.



Friedl KE, Potter AW. Low testosterone is a phenotype of visceral adiposity. *J Endocr Soc.* 2026 Jul 13; 10(8):bvag160. doi.org/10.1210/jendso/bvag160

Changes in parameters related to the risk of cardiometabolic disease were prospectively assessed in a large cohort of young (<35 y.) individuals who have undergone gender-affirming hormone therapy (GAHT) in a Danish centre. Masculinizing GAHT was predominantly associated with long-term adverse changes in lipid status ($\uparrow$ LDL, triglycerides, $\downarrow$ HDL), whereas initializing feminizing GAHT was associated with metabolically unfavourable changes in body composition ($\uparrow$ BMI).



Christensen LL, Palm CV, Andersen MS, T'Sjoen G, Frystyk J, Kristensen TT, Hjortebjerg R, Glintborg D. Prospective Short- and Long-Term Changes in Cardiometabolic Risk Markers Following Gender-Affirming Hormone Therapy. *Andrology.* 2026 Jul 30. doi.org/10.1111/andr.70335

This study compared hormone profiles and testicular histology in 24 persons assigned male at birth, who underwent gender affirming hormone therapy (GAHT). Despite a similar dose of cyproterone acetate, a marked heterogeneity was observed, with different hormone levels and variable suppression of spermatogenesis.

Schiwon K, Sieg F, Schneider F, Hess J, Kliesch S, Schlatt S, Di Persio S, Neuhaus N. Impact of gender-affirming hormone therapy on the endocrine axis and male germ cells. *Reprod Fertil.* 2026 Aug. doi.org/10.1530/raf-26-0032



CYP19A1 encodes aromatase, the enzyme converting androgens to estrogens. This cohort study from the Copenhagen Puberty Study examined associations between *CYP19A1* polymorphisms, circulating sex steroid concentrations, and puberty. In boys, pubertal gynecomastia was linked with *CYP19A1* genotype and was associated with elevated E2 concentrations.



Groendahl VLR, Holmboe SA, Busch AS, Hagen CP, Petersen JH, Johannsen TH, Almstrup K, Frederiksen H, Juul A, Aksglaede L. *CYP19A1* Variation in Healthy Children: Associations with Breast Development and

The European Association of Urology produces an annually updated guideline for the management of testicular cancer. The latest version (2026) highlights the changes compared to the previous version, including: risk factors for stage I seminoma; new evidence on role of RPLND, chemo-radiotherapy, and de-escalated chemotherapy; and new sections on the treatment of bone metastasis, on testicular prosthesis and on rare adult and para-testicular tumors.



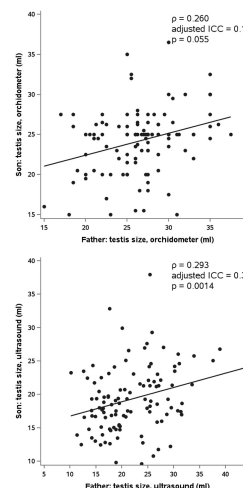
Patrikidou A, Cazzaniga W, Oing C, Berney D, Lobo J, Boormans J, Fankhauser C, Fischer S, Leao R, Gravina C, Nardo DD, Cornes R, Janisch F, Bezuidenhout C, Haugnes HS, Papachristofilou A, Tandstad T, Heidenreich A. European Association of Urology Guidelines on Testicular Cancer: Summary of the 2026 Guidelines. *Eur Urol*. 2026 Aug;90(2):163-174. doi.org/10.1016/j.eururo.2026.03.021

Deep metagenomic profiling of vaginal, seminal, and gut microbiomes was combined with prospective clinical follow-up in two cohorts with reproductive failure (from RUBIC, a multicentre cohort in the Danish-Swedish Øresund region). The study identified microbial factors associated with reproductive outcomes. Seminal dysbiosis and female gut dysbiosis were both consistently associated with prolonged time to livebirth.



Behrendt-Møller I, Krog MC, *et al.* et Rylander L, Jørgensen N, Westergaard D, Almstrup K, Engstrand L, Boulund F, Schuppe-Koistinen I, Vomstein K, Nielsen HS. Gut, vaginal, and seminal microbiomes in couples with infertility or recurrent pregnancy loss: a two-cohort prospective study of reproductive outcomes. *Lancet Obstet Gynaecol Womens Health* 4 Aug 2026, in press. [doi.org/10.1016/S3050-5038\(26\)00213-X](https://doi.org/10.1016/S3050-5038(26)00213-X)

A comparison of reproductive parameters between fathers and sons was performed using data collected in Finland and Denmark. The studied reproductive variables showed weak familial correlations for testicular size, APD, penile width, sperm concentration, and some hormone concentrations. Interestingly, fathers had larger testes and higher sperm concentrations than the sons.



Elamo H, Rodprasert W, Henriksen LS, Jørgensen N, Skakkebaek NE, Juul A, Ollila H, Main KM, Toppari J, Virtanen HE. Father-Son Comparison of Reproductive Traits. *Andrology*. 2026 Aug 18. doi.org/10.1111/andr.70364

This large cross-sectional study found that disrupted calcium homeostasis - characterized by low ionized calcium, elevated PTH, or vitamin D deficiency - is associated with impaired semen quality and altered reproductive hormones. Semen abnormalities included reduced motility, sperm count, and percentage of morphologically normal sperm.



Yahyavi SK, Paredes CE, Homburg M, Jorsal MJ, Jørgensen N, Juul A, Blomberg Jensen M. Calcium deficiency is associated with impaired semen quality in 1230 infertile men. *Reprod Biomed Online*. 2026 Jun 26;53(4):105840. <https://doi.org/10.1016/j.rbmo.2026.105840>

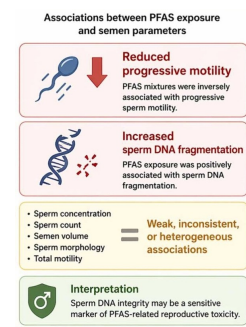
Isotretinoin (ISO) is a retinoid widely used to treat acne. This study combined reproductive function data from a cohort of young men, some treated with ISO, with experimental in vitro exposures of explanted human testis tissue to ISO and retinoic acid.

The findings indicated persistent effects on hormonal parameters (Inhibin B/FSH ratio) in ISO users, supported by changes in hormone secretion observed *in vitro*.

Bendix F, Priskorn L, Jørgensen N, Frederiksen H, Jørgensen A, Mørch L, Ring HC, Kolla SDD, Rosenmai AK, Svingen T, Juul A, Rehfeld A. Isotretinoin use is associated with persistent alterations in male reproductive function. *medRxiv* [PREPRINT] 2026.07.22.26356991; doi: [10.64898/2026.07.22.26356991](https://doi.org/10.64898/2026.07.22.26356991)

This meta-analysis looked carefully upon the postulated associations between PFAS exposure and semen quality. Conventional semen parameters showed heterogeneous and weak associations, however, higher PFAS exposure was consistently associated with increased sperm DNA fragmentation.

Di Nisio A, López-Gil JF, Pizzol D, Ridgell L, Yon DK, Gawronska J, Stellato A, Onal B, De Toni L, Rahmati M, Ravikiran R, Conti L, Trott M, Foresta C, Smith L. Associations between per- and polyfluoroalkyl substances and semen parameters: An updated systematic review and meta-analysis. *J Hazard Mater*. 2026 Sep 1;515:143157. doi:[10.1016/j.jhazmat.2026.143157](https://doi.org/10.1016/j.jhazmat.2026.143157)



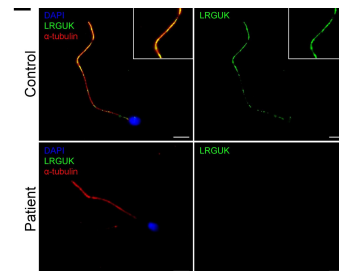
Fungicide chlorothalonil (CHT) is an endocrine disruptor and a potential risk factor for testicular germ cell cancer (TGCC). This study found no overall association between the presence of 4-OH-CHT (a metabolite) in stored maternal pregnancy serum and the risk of TGCC cases in the sons. However, analyses restricted to 1990s pregnancies, when concentrations were higher, suggested increased TGCC risk, particularly for nonseminomas.



Uldbjerg CS, Lindh C, Kristensen DM, Lim YH, Petersen JH, Sørensen KM, Rantakokko P, Coull BA, Bräuner EV, Hauser R, Skakkebæk NE, Juul A, Priskorn L. Concentrations of 4-hydroxychlorothalonil in serum from pregnant women and the association with risk of testicular germ cell cancer in their male offspring. *Environ Res*. 2026 Jul 25;306(Pt 3):125323. doi:[10.1016/j.envres.2026.125323](https://doi.org/10.1016/j.envres.2026.125323)

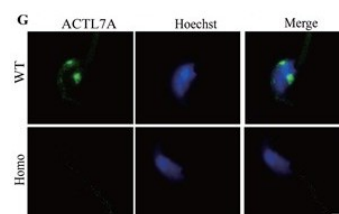
Androgenetics

A novel homozygous truncating variant in LRGUK was identified in an infertile man with a phenotype resembling multiple morphological abnormalities of the flagella (MMAF) but also with sperm head abnormalities. The LRGUK variant was a protein truncating, loss-of-function mutation. IVF-ICSI were attempted in the couple but failed



Mokkedem W, Wehbe Z, Barbotin AL, Boursier A, Tebbakh C, Thierry-Mieg N, Bidart M, Migliaccio A, Chianese R, Arnoult C, Zouari R, Kherraf ZE, Ray PF, Martinez G, Coutton C. Biallelic Truncating Variant in LRGUK Is Associated With Severe Multiple Morphological Abnormalities of the Sperm Flagella and Sperm Nuclear Defects in Humans. *Clin Genet*. 2026 Jul 23. doi:[10.1111/cge.70220](https://doi.org/10.1111/cge.70220)

ACTRT3 variants were identified in two infertile patients with normal sperm concentration and motility. Functional studies in KO mouse showed that sperm with defective ACTRT3 could not initiate calcium oscillations, and defects in ACTRT3 disrupted localization of PLCZ1 in sperm, which resulted in acrosome detachment and fertilization failure



Zhu H, et al et Sang Q. Pathogenic variants in ACTRT3 lead to male infertility characterized by fertilization defects. *Hum Reprod*. 2026 Aug 1;41(8):1350-1366. doi:[10.1093/humrep/deag097](https://doi.org/10.1093/humrep/deag097)

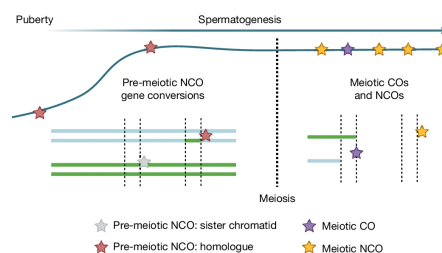
Variants in *FBXO43*, an inhibitor of the anaphase-promoting complex/cyclosome (APC/C) that controls meiotic cell cycle progression, can have different phenotypes. This study found that truncating mutations cause meiotic arrest and NOA, whereas hypomorphic missense mutations permit meiotic completion but result in teratozoospermia (macrozoospermia) with high aneuploidy.

Xiao Y, He Y, Meng L, Zhang H, Tu C, Tan Y, Hu L. Mutation Severity of *FBXO43* Determines Spermatogenic Outcome and Informs Precision ART Strategies. *Hum Mutat*. 2026 Aug 12;2026:7905936. doi.org/10.1155/humu/7905936



Translational and basic andrology

Gene recombination is classically linked to meiosis when double-strand DNA breaks occur at *PRDM9* hotspots, triggering DMC1-mediated crossovers of chromosome fragments. By high-fidelity sequencing of individual sperm and somatic cells, this ground-breaking study found that a substantial proportion of gene conversion occurs before meiosis (without crossovers), e.g. in spermatogonia, during DNA repair in response to damage, and the changes are transmitted to the next generation.



Schweiger R, Lee S, Zhou C, Yang TP, Li S, Sanghvi R, Neville M, Smith K, Roberts K, Nessa A, Wadge S, Small KS, Campbell PJ, Almstrup K, Sudmant PH, Rahbari R, Durbin R. Long-read sequencing reveals pre-meiotic gene conversion in sperm. *Nature*. 2026 Aug 26. doi.org/10.1038/s41586-026-10901-0

Testis tissue from patients with prostate cancer treated with androgen deprivation therapy (ADT) was used to analyse androgen regulation in Sertoli cells by single-nucleus RNA sequencing, single-cell ATAC-seq, and spatial transcriptomics.

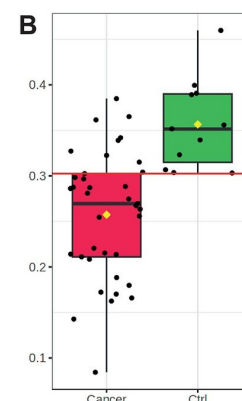
The study identified Neuregulin 2 (*NRG2*) as an androgen-dependent Sertoli cell factor that promotes spermatogonial proliferation. ADT caused ectopic expression *WT1* in the interstitium, reprogramming a subset of interstitial cells toward a Sertoli-like transcriptomic state.



Guo Y, Xu K, *et al.* et Guo J, Multi-omic analysis of androgen-deprived human testes reveals Sertoli cell regulation and niche reprogramming. *Nat Commun* (2026) – in press. <https://doi.org/10.1038/s41467-026-76120-3>

The seminal plasma metabolome in patients with testicular germ cell tumours (TGCT) vs controls was characterized using a multi-platform metabolomics strategy that covers polar metabolites and oxylipins. Detectable metabolic signatures of TGCT in seminal plasma were identified, encompassing alterations in energy metabolism and inflammation-related lipid mediators.

Alonso-Dasques L, Mamani-Huanca M, Camunas-Alberca SM, Mørup N, Winge SB, Fernández-Hernández C, López-González Á, Rupérez FJ, García A, Rudaz S, Nef S, Taha AY, Almstrup K, Barbas C, González-Ruiz V. Metabolic and Oxylipin Signature of Testicular Germ Cell Tumors in Seminal Plasma. *Andrology*. 2026 Aug 9. doi: 10.1111/andr.70347.



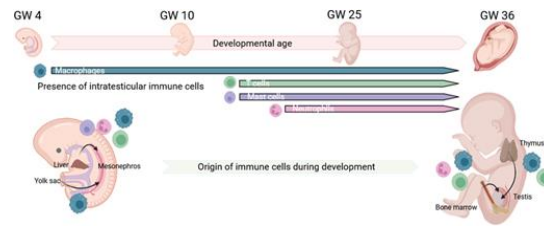
Stress conditions elicit the formation of stress granules (SGs) in germ cells. This study found that *ATXN2* is a main component of heat-induced SGs and identified a unique population of *ATXN2*-positive SGs in spermatocytes.

ATXN2-positive granules increased in the absence of *TENT5A* (a cytoplasmic poly(A) polymerase), reducing apoptosis in late pachytene spermatocytes, and rescuing fertility following heat exposure.



Chi RA, Gupta A, Li Y, Baptissart M, Lee D, Papas BN, Morgan M. The TENT5A-ATXN2 axis modulates germline and somatic cell survival during heat stress. *Cell Death Dis.* 2026 Jul 24. doi.org/10.1038/s41419-026-09086-1

This study provided a detailed localization and potential roles of immune cells (macrophages, T cells, neutrophils, and mast cells) during fetal development of human testis and epididymis.



Similar to mice, the early stage macrophage abundance, preceding bone marrow hematopoiesis, suggested yolk sac and/or liver origins, while later-appearing immune cells are likely bone marrow-derived.

Hosseini S, Jezek D, Kos M, Nathaniel B, Rajpert-De Meyts E, Hedger MP, Schuppe HC, Loveland KL, Fietz D. Localisation of immune cell populations during fetal human testicular development. *Reprod Fertil.* 2026 Jul 1;7(3):RAF250189. doi.org/10.1530/RAF-25-0189

A flurry of excellent studies providing novel information on **sperm biology** appeared recently as preprints (not yet peer-reviewed). Here they are for your perusal:



Hammoud S, Rabbani M, Apell Z *et al* et Cairns B, Kim M, Wilson T. Higher-order genome architecture of spermatids guides chromatin assembly in mature sperm. *Research Square* [PREPRINT] July 2026, <https://doi.org/10.21203/rs.3.rs-10308188/v1>

Nishio S, Wang H, Jovine L. How a single sperm protein recognizes highly divergent egg coat components. *BioRxiv* [PREPRINT] August 2026, <https://doi.org/10.64898/2026.07.29.741504>



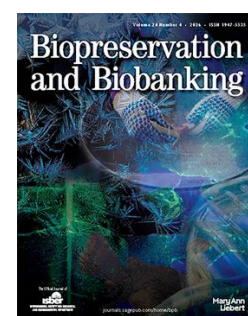
Wang Z, Wang H, Magalhaes RDM *et al.* et Zheng H, Yan W. Life without cytoplasm: sperm sustain protein production utilizing cytoplasmic droplets and mitochondria as translational apparatuses. *BioRxiv* [PREPRINT] August 2026, <https://doi.org/10.64898/2026.08.10.744062>

Chen S, Magalhaes RDM, Wang Z, *et al.* et Wang C, Swerdloff RS, McCarrey JR, Zheng H, Yan W. Paternal Metabolic Reversal Remodels Sperm RNA Profiles and Ameliorates Intergenerational Metabolic Disorder in Mice. *BioRxiv* [PREPRINT] August 2026, <https://doi.org/10.64898/2026.07.31.742153>

New research resource

For those of you working with nonhuman primates – the NIH-funded Developmental Genotype-Tissue Expression (dGTEx) will include fetal and adult tissues and data from Rhesus Macaque and Marmoset provided by the renown Oregon National Primate Research Center (USA).

Castro JN, Silva de Castro S, Linn RL, Van Hoose PM, Anderson L, Ardlie KG, Conrad DF, Lewis AD, Roberts VHJ. The Nonhuman Primate Developmental Genotype-Tissue Expression Biospecimen and Histopathology Resource. *Biopreserv Biobank.* 2026 Aug 6:19475535261475862. doi.org/10.1177/19475535261475862



Andrology lab

It is time to move on from the widely used density gradient centrifugation (DGC) of sperm.

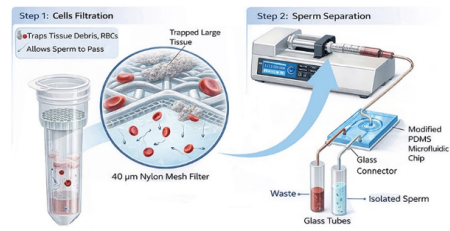
This study recommends using the micro swim-up (MSU) approach, which markedly reduced DNA fragmentation and improved chromatin maturation.

ANDROLOGY



Palini S, Benedetti S, De Stefani S, Galluzzi L, Primiterra M, D'Errico SR, Tanturli M, Muratori M. Sperm Selection Using Micro Swim-Up: Improvement of Chromatin Integrity Compared to Density Gradient Centrifugation. **Andrology**. 2026 Jul 29. doi.org/10.1111/andr.70327

A microfluidic platform for rapid sperm isolation from biopsy-derived material is presented in this study. After pre-filtration of tissue fragments, an inertial spiral microfluidic device separates cells by size, preserving sperm motility, morphology, and DNA integrity.



Maleki M, Mosaddegh P, Nasr Esfahani MH, Sadeghian G, Pischevar A, Nosrati R. Sperm recovery from testicular biopsies containing tissue fragments and other somatic cells, using an inertial spiral microfluidic chip. **Lab Chip**. 2026 Aug 7. <https://doi.org/10.1039/d6lc00395h>

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