International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	IMPACT OF COMMON CHRONIC DISEASES ON SEMEN QUALITY: A NARRATIVE REVIEW
DOI	https://doi.org/10.31435/ijitss.2(50).2026.5223
RECEIVED	14 February 2026
ACCEPTED	27 March 2026
PUBLISHED	06 April 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

IMPACT OF COMMON CHRONIC DISEASES ON SEMEN QUALITY: A NARRATIVE REVIEW

Wiktor Śliwiński *(Corresponding Author, Email: wiktorsliwinski2000@gmail.com)*
The Independent Public Healthcare Institution of the Ministry of the Interior and Administration in Łódź, Łódź, Poland
ORCID ID: 0009-0003-3584-9776

Dominika Matecka
Józef Struś Municipal Hospital, Multispecialty Medical Centre, Poznań, Poland
ORCID ID: 0009-0000-4644-5943

Jakub Mazur
Voivodeship Combined Hospital in Kielce, Kielce, Poland
ORCID ID: 0009-0005-1089-9210

Daniel Chołuj
The Independent Public Healthcare Institution of the Ministry of the Interior and Administration in Łódź, Łódź, Poland
ORCID ID: 0009-0009-1445-6336

Weronika Pura
The Independent Public Healthcare Institution of the Ministry of the Interior and Administration in Łódź, Łódź, Poland
ORCID ID: 0009-0007-2889-667X

Karolina Zarówna
District Hospital Complex in Oleśnica, Oleśnica, Poland
ORCID ID: 0009-0003-6066-7667

Mateusz Kosowski
Independent Public Healthcare Institution in Koło, Koło, Poland
ORCID ID: 0009-0001-0811-5326

Jakub Marciniak
University Clinical Hospital No. 2 of the Medical University of Łódź, Łódź, Poland
ORCID ID: 0009-0004-5675-6963

ABSTRACT

Background. Chronic diseases, including obesity, type 2 diabetes, cardiovascular diseases, and autoimmune conditions, represent a significant threat to male fertility. These conditions disrupt testicular homeostasis through interconnected pathophysiological mechanisms, leading to the deterioration of semen parameters and sperm genomic integrity.
Aim. This narrative review aims to analyze the impact of common chronic diseases on semen quality and to discuss the integrated molecular and systemic mechanisms underlying male infertility in these clinical conditions.
Material and methods. A narrative review of current scientific literature was conducted, focusing on clinical and experimental studies regarding the effects of metabolic, cardiovascular, autoimmune, renal, and hepatic disorders on male reproductive functions. Key pathomechanisms, including oxidative stress, inflammation, and hormonal dysregulation, were analyzed.
Results. Five primary pathways leading to testicular dysfunction were identified: (1) oxidative stress causing lipid peroxidation and decreased sperm motility; (2) chronic inflammation disrupting the blood-testis barrier; (3) HPG axis dysregulation leading to hypogonadism; (4) endothelial dysfunction impairing testicular microcirculation and thermoregulation; and (5) sperm DNA damage. It was shown that patients with diabetes, hypertension, and inflammatory joint diseases exhibit significantly lower sperm concentration, volume, and motility compared to control groups.
Conclusions. Chronic diseases exert a multidirectional, negative impact on semen quality, and the degree of fertility impairment often correlates with disease activity and stage. Management of metabolic and cardiovascular health, along with inflammatory control, is crucial for preserving male reproductive potential.

KEYWORDS

Male Infertility, Semen Quality, Chronic Diseases, Oxidative Stress, Metabolic Syndrome

CITATION

Wiktor Śliwiński, Dominika Matecka, Jakub Mazur, Daniel Chołuj, Weronika Pura, Karolina Zarówna, Mateusz Kosowski, Jakub Marciniak. (2026) Impact of Common Chronic Diseases on Semen Quality: A Narrative Review. *International Journal of Innovative Technologies in Social Science*. 2(50). doi: 10.31435/ijitss.2(50).2026.5223

1 Pathophysiological Mechanisms contributing to decreased semen quality

1.1 Oxidative stress

Chronic diseases disrupt the balance between reactive oxygen species (ROS) production and antioxidant capacity in the testis. While ROS are normally generated through mitochondrial metabolism and serve essential signaling functions in sperm capacitation and acrosome reaction (Wang et al., 2025), excessive ROS production overwhelms intrinsic testicular antioxidant defenses—including superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx)—causing progressive spermatozoal and somatic cell dysfunction (Patan et al., 2025). Spermatozoa are particularly vulnerable to oxidative damage due to their plasma membrane's exceptionally high polyunsaturated fatty acid (PUFA) content, making them prime targets for ROS-induced lipid peroxidation. This process damages membrane composition and fluidity, increasing permeability and functional loss. In the mitochondria-rich midpiece, lipid peroxidation dissipates membrane potential, impairs ATP synthesis, and reduces motility. Secondary metabolites such as 4-hydroxynonenal (4-HNE) and malondialdehyde (MDA) further dysregulate bioenergetic proteins and damage axonemal structures critical for flagellar function (Nowicka-Bauer & Nixon, 2020). The pro-oxidant/antioxidant imbalance in chronic disease operates through multiple mechanisms: obesity promotes ROS via enhanced NADPH oxidase activity and uncoupled eNOS (Mosanezhad et al., 2025), while type 2 diabetes induces hyperglycemia-driven ROS generation through advanced glycation end products (AGEs) (Dutta et al., 2021). Simultaneously, antioxidant enzyme expression—SOD, GPx, and catalase—becomes downregulated in testicular tissue and seminal plasma (S et al., 2025).

1.2 Chronic inflammation

Chronic systemic inflammation is a hallmark feature of obesity, metabolic syndrome, type 2 diabetes, cardiovascular disease, and chronic kidney disease, with direct consequences for testicular homeostasis (Fang et al., 2021). The inflammatory milieu is characterized by sustained elevation of pro-inflammatory cytokines—particularly tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6)—produced by immune cells, adipose tissue, vascular endothelium, and testicular cells including resident macrophages and Leydig cells (Potiris et al., 2025). These cytokines mediate gonadotoxic effects through receptor binding on seminiferous epithelial cells, spermatogonia, and other testicular somatic cells (Guazzone et al., 2009). The testicular immune microenvironment normally maintains immune privilege—a specialized immunosuppressive state protecting germ cells from autoimmune attack (Li et al., 2012). However, chronic inflammatory states compromise this balance by inducing aberrant adhesion molecule expression and disrupting the blood-testis barrier (BTB)—the critical tight junction interface between Sertoli cells (Elmas et al., 2022). TNF-α and IL-6 promote phosphorylation and internalization of claudin-11 and occludin, increasing paracellular permeability and leukocyte infiltration (Fang et al., 2021). Chronic inflammation also dysregulates anti-inflammatory mediators—transforming growth factor-beta (TGF-β) and interleukin-10 (IL-10)—normally expressed by Sertoli cells and resident macrophages (Loveland et al., 2017). The influx of activated leukocytes into the testicular interstitium and seminiferous tubules amplifies oxidative stress through massive ROS and reactive nitrogen species (RNS) production, creating a pathological feedback loop wherein inflammation-driven oxidative stress further exacerbates barrier dysfunction (Dutta et al., 2021). Circulating pro-inflammatory cytokines also directly impair spermatogenesis by promoting apoptosis of developing germ cells through TNF-α receptor 1 (TNFR1) and IL-6 receptor signaling, which activate caspase-dependent cell death pathways (Guazzone et al., 2009). Furthermore, elevated systemic IL-6 and TNF-α are associated with reduced testosterone production from Leydig cells and impaired synthesis of anti-Müllerian hormone (AMH) from Sertoli cells, thereby disrupting the endocrine regulation of spermatogenesis (Loveland et al., 2017).

1.3 Hormonal dysregulation

Chronic diseases trigger comprehensive dysregulation of the hypothalamic-pituitary-gonadal (HPG) axis, resulting in functional hypogonadism that impairs both testosterone synthesis and spermatogenesis. The HPG axis operates through pulsatile gonadotropin-releasing hormone (GnRH) secretion from the hypothalamus, which stimulates luteinizing hormone (LH) and follicle-stimulating hormone (FSH) release from the anterior pituitary; these gonadotropins then drive testicular steroidogenesis and spermatogenesis through receptor signaling on Leydig and Sertoli cells, respectively (Corona et al., 2023). In obesity and metabolic syndrome, hyperinsulinemia and insulin resistance directly suppress GnRH pulsatility through altered intracellular signaling in hypothalamic neurons, reducing downstream LH and FSH secretion (Jaramillo et al., 2025). Concurrently, elevated leptin levels in obesity paradoxically induce central leptin resistance despite high circulating concentrations, blunting the normally stimulatory effects of leptin on GnRH neurons, further depressing gonadotropin secretion (Elias & Purohit, 2012). The disruption of the HPG axis in chronic diseases is compounded by dysregulation of peripheral testosterone metabolism. Insulin resistance and obesity-associated hyperinsulinemia enhance 5-alpha reductase and aromatase activity, with excess aromatase converting testosterone to 17-β-estradiol, thereby reducing bioavailable testosterone while elevating circulating estrogen levels (Rabijewski, 2023). This altered sex steroid ratio suppresses GnRH secretion through enhanced negative feedback, creating a feed-forward mechanism that perpetuates hypogonadism (Mahmood et al., 2025). Additionally, chronic inflammation reduces the expression and sensitivity of gonadotropin receptors on Leydig cells, impairing the testosterone-stimulating effects of LH despite normal or elevated LH levels—a phenomenon termed secondary hypogonadotropic hypogonadism. Type 2 diabetes induces particular severity in HPG axis dysfunction, as hyperglycemia directly impairs Leydig cell steroidogenesis through enhanced oxidative stress, mitochondrial dysfunction, and impaired expression of steroidogenic enzymes including P450scc and 17β-HSD (Huang et al., 2024). The hormonal consequences extend beyond testosterone suppression to encompass impaired spermatogenesis through FSH-mediated mechanisms. Reduced FSH secretion and diminished FSH receptor responsiveness in Sertoli cells impair the proliferation, differentiation, and survival of germ cells (Ye et al., 2021). Obesity-associated adipokine dysregulation—characterized by elevated leptin, reduced adiponectin, and increased resistin—further disrupts spermatogenesis through direct effects on testicular cells and through systemic metabolic signaling (Gabriel et al., 2025).

1.4 Endothelial dysfunction

The systemic endothelial dysfunction characteristic of chronic diseases fundamentally impairs the specialized vascular homeostasis required for optimal testicular function and spermatogenesis. Nitric oxide (NO), generated through eNOS activity in vascular endothelium, serves as a critical vasodilator regulating microvascular blood flow, maintains antiplatelet and anti-inflammatory properties, and plays essential roles in testicular vascular hemodynamics (Pandian et al., 2024). In obesity, metabolic syndrome, and type 2 diabetes, reduced eNOS expression and activity result from multiple mechanisms including diminished eNOS phosphorylation, impaired tetrahydrofolate (BH4) cofactor availability, and enhanced eNOS uncoupling that generates superoxide rather than NO (Kwaifa & Noor, 2024). The decreased bioavailable NO is further exacerbated by rapid scavenging through reaction with superoxide anions to form peroxynitrite (ONOO-), a potent oxidant that promotes protein nitrosylation and further oxidative damage (Penna & Pagliaro, 2025). The consequence of reduced testicular NO bioavailability is profound: impaired microvascular vasodilation leads to diminished capillary recruitment and reduced blood flow through testicular tissue, compromising oxygen and nutrient delivery to spermatogonia and supporting Sertoli cells (Kwaifa & Noor, 2024). Obesity-induced adipose tissue accumulation surrounding the testes, combined with systemic endothelial dysfunction, amplifies local microvascular insufficiency and exacerbates oxidative stress within the seminiferous tubules (Virdis et al., 2018). Furthermore, the normal thermoregulatory capacity of the testicular microvasculature is severely impaired when eNOS-mediated vasodilation is compromised; this is particularly consequential since spermatogenesis requires temperatures approximately 1-2°C below core body temperature, achieved through efficient heat exchange between the pampiniform plexus and testicular interstitium (Pandian et al., 2024). Chronic endothelial dysfunction prevents appropriate temperature regulation, subjecting spermatogenic cells to chronically elevated temperatures that accelerate oxidative stress and promote germ cell apoptosis (Lai et al., 2022). The endothelial dysfunction in chronic diseases also involves enhanced NADPH oxidase (NOx) activity and increased ROS production by endothelial cells, which synergistically with reduced NO bioavailability creates a profoundly pro-oxidant microvascular environment (Penna & Pagliaro, 2025). Increased TNF-α and IL-6 signaling further impairs endothelial function through activation of NF-κB, which downregulates eNOS expression and upregulates NADPH oxidase subunits (Aleksandrowicz et al., 2025). The resulting vascular inflammation, characterized by enhanced expression of intercellular adhesion molecules (ICAM-1) and vascular cell adhesion molecules (VCAM-1), promotes leukocyte infiltration and amplifies the inflammatory cascade within testicular tissue (Donato et al., 2009).

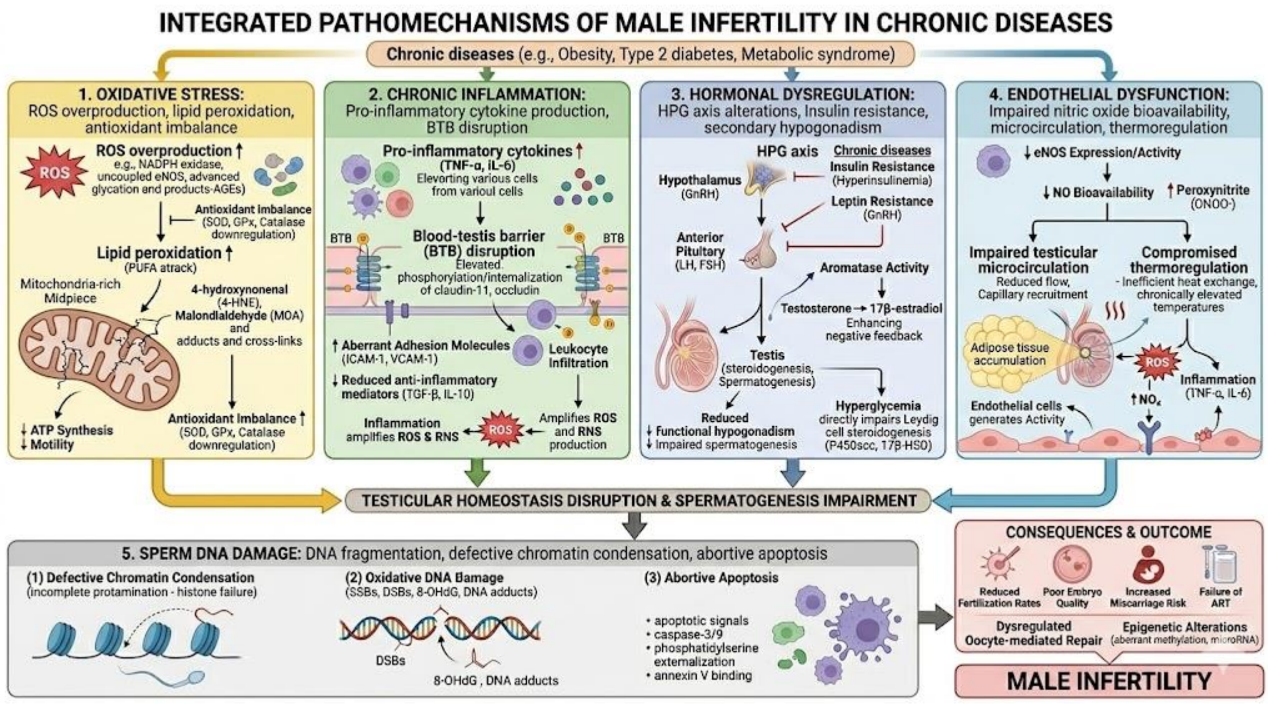

Fig. 1.

Figure 1. Integrated pathophysiological mechanisms of male infertility in chronic diseases. Chronic conditions (e.g., obesity, type 2 diabetes) disrupt testicular homeostasis through five interconnected pathways: (1) Oxidative stress: ROS overproduction and antioxidant imbalance cause lipid peroxidation, impairing sperm motility and ATP synthesis. (2) Chronic inflammation: Pro-inflammatory cytokines (TNF-α, IL-6) disrupt the blood-testis barrier (BTB) and promote leukocyte infiltration. (3) Hormonal dysregulation: HPG axis alterations, insulin resistance, and increased aromatase activity lead to secondary hypogonadism and reduced testosterone bioavailability. (4) Endothelial dysfunction: Impaired nitric oxide (NO) signaling compromises testicular microcirculation and thermoregulation. (5) Sperm DNA damage: These upstream insults converge to cause defective chromatin condensation, oxidative DNA lesions (e.g., 8-OHdG), and abortive apoptosis. Ultimately, these integrated dysfunctions result in compromised genomic integrity, poor embryo quality, and adverse reproductive outcomes.

2. Chronic conditions and their specific effects on male fertility

2.1 Metabolic Disorders (Obesity, Type 2 Diabetes Mellitus, Metabolic Syndrome)

Metabolic disorders including obesity, type 2 diabetes mellitus, and metabolic syndrome substantially impair male reproductive health through multiple interconnected mechanisms. Type 2 diabetes mellitus significantly impairs male reproductive health largely through hyperglycemia-induced oxidative stress, which depletes antioxidant defenses and generates reactive oxygen species that directly damage spermatozoa, resulting in reduced motility, abnormal morphology, DNA fragmentation, and disrupted membrane integrity (Sm et al., 2025). The condition also compromises the hypothalamic-pituitary-gonadal axis, lowering testosterone synthesis and impairing spermatogenesis, while chronic inflammation and advanced glycation end products formation further exacerbate dysfunction of Leydig and Sertoli cells, leading to testicular apoptosis and microvascular injury (Sm et al., 2025). Clinical evidence demonstrates that infertile men with type 2 diabetes mellitus have significantly lower sperm volume and substantially decreased sperm motility compared to non-diabetic controls (R et al., 2026). Additionally, type 2 diabetes mellitus impairs spermatogenesis through multiple molecular mechanisms including oxidative stress, endocrine disruption, dysregulated gene expression, metabolic imbalance, and mitochondrial dysfunction, with some evidence suggesting that even men with seemingly normal semen parameters may exhibit hidden sperm DNA damage if diabetic (A et al., 2025). Obesity is associated with hormonal imbalance, increased oxidative stress, and inflammation in the testis, which adversely affect sperm quality and lead to impaired male fertility (Eo et al., 2025). The condition impairs spermatogenesis through aromatase-mediated hormonal imbalance and inflammation, with obesity directly reducing sperm dynamics and morphological parameters—including reduced sperm count, concentration, and motility—while increasing sperm DNA fragmentation index compared to non-obese populations (D et al., 2025). Additionally, obesity-induced changes in immune function lead to testicular dysfunction and impaired spermatogenesis through chronic low-grade inflammation, immune cell infiltration, and dysregulation of adipokines such as leptin and adiponectin (R et al., 2025). The impairment of spermatogenesis in obese males occurs in part through reduced Sertoli cell lactate and NAD+ production, metabolic imbalances affecting the testicular microenvironment (K et al., 2025). Research demonstrates a moderate-strength positive correlation between metabolic dysfunction scores and sperm DNA fragmentation index, with metabolic syndrome showing statistically significant associations with abnormal sperm DNA fragmentation (D & J, 2025). Beyond sperm DNA damage, metabolic syndrome amplifies oxidative stress and further impairs fertility potential through dysregulation of immunometabolic pathways, wherein systemic metabolic inflammation enhances glycolysis while suppressing oxidative phosphorylation and promoting accumulation of reactive oxygen species in testicular tissues (J et al., 2025). These findings underscore the critical importance of managing metabolic health for maintaining male reproductive function and fertility potential.

2.2 Patophysiology of decreased semen quality in cardiovascular diseases

2.2.1 Vascular and Mitochondrial Dysfunction

The principal pathway through which cardiovascular disease deteriorates semen quality involves vascular impairment. Cardiovascular conditions induce abnormalities in testicular microcirculation, thereby limiting oxygen supply to testicular tissue. This circulatory insufficiency directly injures the seminiferous epithelium, which has high metabolic demands. Moreover, hypertension-related vascular disturbances contribute to mitochondrial dysfunction in spermatozoa, intensifying oxidative stress that damages sperm DNA and reduces motility (Colli et al., 2019).

2.2.2 Oxidative Stress

Cardiovascular disorders enhance oxidative stress beyond the antioxidant defense capacity of sperm cells. Although reactive oxygen species (ROS) are essential for normal sperm physiology—including processes such as capacitation—excessive ROS levels initiate oxidative injury to sperm membranes and genetic material (Costa et al., 2023). Non-communicable diseases, including cardiovascular disease, further disrupt mitochondrial activity in sperm, resulting in diminished motility, lower concentration, and decreased viability.

2.2.3 Hormonal Dysregulation

Cardiovascular pathology interferes with the hypothalamic–pituitary–gonadal (HPG) axis, leading to reduced testosterone synthesis. Decreased testosterone levels are commonly observed in men with cardiovascular-related testicular dysfunction and contribute to erectile dysfunction and diminished libido (Kaltsas et al., 2025). This endocrine imbalance further impairs spermatogenesis and sexual performance.

2.2.4 Link Between Erectile Dysfunction and Cardiovascular Health

A significant clinical observation is that erectile dysfunction functions as an indicator of both overt and subclinical cardiovascular disease (Silva & Anderson, 2022). A well-documented association exists between erectile dysfunction and subsequent adverse cardiovascular events (Hart, 2023), suggesting that reproductive impairment and cardiovascular pathology frequently coexist and share common underlying mechanisms. This reciprocal relationship highlights the close interdependence between vascular integrity and reproductive capability.

2.2.5 Hypertension and Semen Quality

Cardiovascular disease exerts substantial adverse effects on male reproductive potential, influencing various parameters of semen quality through both direct testicular mechanisms and broader systemic pathophysiological pathways.Arterial hypertension, which affects approximately 700 million men of reproductive age, compromises semen quality via multiple pathways (Colli et al., 2019). Studies indicate that men with hypertension have an elevated risk of reproductive complications, including erectile dysfunction. This disorder leads to structural changes in the testes, mainly as a result of vascular abnormalities and disrupted testicular blood flow regulation. In experimental animal models, hypertensive rats exhibited reduced sperm concentration, impaired DNA integrity, and markedly higher proportions of spermatozoa with dysfunctional mitochondria and abnormal morphology (Colli et al., 2019).

2.2.6 Clinical Implications

Current evidence suggests that cardiovascular disease should be acknowledged as a major risk factor for male infertility. Men diagnosed with hypertension and metabolic syndrome warrant thorough evaluation, including analysis of semen parameters and assessment of sexual health. Addressing and controlling cardiovascular risk factors—such as optimizing blood pressure, managing body weight, and mitigating oxidative stress—may represent effective strategies for safeguarding male fertility in individuals affected by cardiovascular disease.

2.3 Impact of Chronic Autoimmune diseases on semen quality

Autoimmune disorders markedly impair male reproductive function through persistent inflammatory processes that directly hinder spermatogenesis and disturb hormonal balance. These consequences are particularly significant because many autoimmune conditions arise during peak reproductive years. Autoimmune diseases affect approximately 5–8% of the global population and are increasingly acknowledged as factors compromising male fertility (Finelli et al., 2021). They represent some of the most frequent medical comorbidities among men with abnormal semen parameters, occurring in 16.9% of men with oligospermia and 15.7% of those with azoospermia, compared with 13.2% in men presenting normal semen profiles (Fendereski et al., 2024).

The immune system plays a dual role in male reproduction, safeguarding and regulating reproductive organs while maintaining testicular immune privilege (Ma et al., 2024). In autoimmune disease, sustained or intensified inflammation disrupts this equilibrium, leading to immune-mediated injury of reproductive tissues. The outcome includes diminished sperm production, inferior sperm quality, and reduced gonadal hormone secretion. The systemic inflammatory environment characteristic of autoimmune disorders directly damages the seminiferous epithelium and interferes with spermatogenesis (Scriffignano et al., 2024). Accumulation of immune cells and elevated proinflammatory cytokines—such as TNF-ff, IL-1, and IL-6—within reproductive tissues induces germ cell apoptosis and lowers cellular viability. Autoimmune diseases provoke excessive oxidative stress that surpasses the antioxidant defenses of sperm cells (Ma et al., 2024). This imbalance results in DNA injury, membrane instability, and reduced motility and morphological integrity.

2.3.1 Inflammatory Arthritis

Men diagnosed with inflammatory arthritis—including Rheumatoid arthritis, Spondyloarthritis, Ankylosing spondylitis, and Psoriatic arthritis—exhibit substantial deterioration across key semen parameters. Disease activity showed a significant inverse relationship with semen quality, indicating that greater inflammatory burden corresponded to poorer sperm parameters (Aziz et al., 2025). Erectile dysfunction was also more prevalent, affecting 35% of patients compared with 12.5% of controls.

Table 1.

	Affected individuals	Healthy controls
Lower semen volume	2.1 mL	2.6 mL
Reduced sperm concentration	31.4 million/mL	48.5 million/mL
Decreased progressive motility	39.2%	52.6%
Increased morphological abnormalities	3.6%	5.4%

Table presents a comparative analysis between affected individuals and healthy controls (Aziz et al., 2025).

2.3.2 Systemic lupus erythematosus (SLE)

SLE, a multisystem autoimmune condition, exerts a profound negative effect on male reproductive health. Men with SLE demonstrate markedly increased erectile dysfunction, elevated gonadotropins: significantly higher FSH and LH and reduced total sperm count (Zhu et al., 2025). Men with SLE also present altered semen characteristics, including increased DNA fragmentation, which may adversely influence assisted reproductive outcomes (Waters et al., 2020).

2.3.3 Spondyloarthritis Spectrum Disorders

Male fertility has become an important concern in Spondyloarthritis (SpA), Ankylosing spondylitis (AS), and Psoriatic arthritis (PsA) (Scriffignano et al., 2024). These chronic inflammatory rheumatic diseases can interfere with family planning, particularly when diagnosed at a young age. Strong evidence links elevated disease activity with greater impairment of sperm quality.

2.3.4 Vasculitis

Vasculitis, defined by inflammation of blood vessels, contributes to erectile dysfunction and male infertility through diverse mechanisms (Keskin & Altan, 2025). Affected individuals may experience: persistent inflammation with vascular involvement, hormonal disturbances, reduced erectile capacity and fertility, high prevalence of hypogonadism and sexual dysfunction in subtypes such as Granulomatosis with polyangiitis and Behçet's disease.

2.3.6 Effects of Disease-Modifying Therapy

Table 2.

Medications used in immune treatment	Influence on male reproductive system
Biologic agents, particularly TNF inhibitors	favorable reproductive safety profile, with improved fertility parameters observed in treated patients
TNF inhibitors	reassuring effects on semen quality in clinical investigations (Scriffignano et al., 2024)
Conventional DMARDs and NSAIDs	comparatively less favorable fertility outcomes
Methotrexate	recent studies indicate no statistically significant short-term adverse impact on semen parameters in men with psoriasis (Elhanbly et al., 2025)
Corticosteroids and other immunosuppressants	may negatively influence semen quality and, in some cases, pose teratogenic risks (Keskin & Altan, 2025).

Table 2 presents therapeutic strategies for autoimmune diseases exert variable influences on male fertility (Aziz et al., 2025).

2.4 Chronic Kidney and liver disease impact on semen quality

2.4.1 Chronic Kidney Disease (CKD) and Semen Quality

In a large longitudinal analysis of over 2,000 patients, chronic kidney disease was associated with lower sperm concentrations and reduced total motile sperm (Scott et al., 2024). Specifically, higher CKD stages show a clear dose-dependent relationship with worsening semen parameters, including reduced semen volume, progressive motility, sperm concentration, and total sperm number (Lehtihet & Hylander, 2015).

The mechanisms underlying this impairment are multifactorial. CKD and hemodialysis (renal replacement therapy) are associated with vascular, hormonal, and structural alterations that impair reproductive function (Kariev et al., 2026). Men with CKD show decreased serum testosterone levels, reduced luteinizing hormone and follicle-stimulating hormone, and increased rates of abnormal spermatogenesis patterns including asthenozoospermia, oligozoospermia, and combined defects (Kariev et al., 2026). Additionally, elevated levels of specific biomarkers like microRNA-155 in men with CKD stages 1-4 were associated with lower sperm concentration and total sperm number, suggesting these may serve as early markers of subfertility (Eckersten et al., 2017).

The good news is that kidney transplantation can partially reverse these effects. Following kidney transplantation, erectile function improved significantly in most patients, and the proportion of men with normal sperm parameters (normozoospermia) increased from 37.3% to 61.2%, with one case even documenting natural conception after transplantation in a previously azoospermic man (Nguyen et al., 2025).

2.4.2 Chronic Liver Disease and Reproductive Health

Research specifically examining the impact of chronic liver disease on semen quality is more limited compared to kidney disease data. However, available evidence suggests reproductive complications do occur. In patients with chronic hepatitis B-related liver cirrhosis, the prevalence of erectile dysfunction was significantly higher (41.2%) compared to those with chronic hepatitis B without cirrhosis (8.6%), suggesting that advancing liver disease severity affects sexual and reproductive function (Kim et al., 2015). For men requiring antiviral therapy for hepatitis C (sofosbuvir and ribavirin), both agents caused a significant decrease in total sperm motility percentage, indicating that both the liver disease and its treatments can compromise fertility (Ali et al., 2024).

2.5 Impact of endocrine disorders on semen quality

While multiple etiological factors contribute to male subfertility, endocrine dysfunction has emerged as a critical and often modifiable cause of impaired semen quality. The normal regulation of male reproductive function depends on a precisely orchestrated hormonal axis: the hypothalamic-pituitary-gonadal (HPG) axis, which coordinates testosterone production and spermatogenesis (Dutta et al., 2019). Any disruption at any level of this axis—whether from thyroid disorders, diabetes mellitus, hypogonadism, or obesity—can have profound consequences on semen parameters and male fertility potential.

2.5.1 Thyroid Disorders and Semen Quality

Thyroid hormones play crucial regulatory roles in male reproductive physiology beyond their classical metabolic functions. The thyroid hormones—thyroxine (T4) and triiodothyronine (T3) regulate testicular development, maintenance of spermatogenic function, and the overall neuroendocrine axis governing male reproduction (Sengupta & Dutta, 2018). Both excess and deficiency of thyroid hormones can significantly alter semen quality through direct and indirect mechanisms.

2.5.2 Hypothyroidism and Reproductive Dysfunction

Hypothyroidism, characterized by insufficient thyroid hormone production, leads to reduced metabolic activity and a cascade of hormonal changes affecting the HPG axis. In hypothyroid states, the crosstalk between the hypothalamic-pituitary-thyroid (HPT) axis and the HPG axis becomes disrupted, resulting in altered gonadotropin secretion and consequently decreased testosterone levels (Sengupta & Dutta, 2018). Studies demonstrate that hypothyroid men frequently present with decreased total sperm count, reduced sperm motility, and increased abnormal sperm morphology. The seminal plasma composition is also altered in hypothyroidism, with modifications in fructose content and other essential nutrients supporting sperm function.

2.5.3 Hyperthyroidism and Testicular Function

Conversely, hyperthyroidism—characterized by excessive thyroid hormone production—also impairs semen quality through different mechanisms. The hypermetabolic state associated with hyperthyroidism increases cellular oxidative stress and energy expenditure, potentially overwhelming the antioxidant defense systems of spermatozoa. Additionally, elevated thyroid hormone levels can suppress luteinizing hormone (LH) and follicle-stimulating hormone (FSH) secretion, thereby reducing testosterone synthesis and impairing spermatogenesis.

2.5.4 Hypogonadism and Testosterone Deficiency

Male hypogonadism, defined as inadequate testosterone production by Leydig cells, represents one of the most direct endocrine causes of male infertility. Both primary hypogonadism (testicular failure) and secondary hypogonadism (central dysfunction of GnRH, FSH, or LH secretion) significantly compromise semen quality through loss of the hormone essential for spermatogenesis, sexual function, and overall reproductive health. Testosterone is absolutely essential for normal spermatogenesis. Produced primarily by Leydig cells in response to LH stimulation, testosterone acts directly on germ cells through androgen receptors, supporting their development through meiosis and maintaining their motility and viability. In hypogonadal men with total testosterone levels below 350 ng/dL, spermatogenesis is profoundly compromised, resulting in oligozoospermia (reduced sperm count), asthenozoospermia (reduced motility), and teratozoospermia (morphological abnormalities). Men with functional hypogonadism—characterized by low-normal testosterone in association with symptoms—present with particularly challenging diagnostic and therapeutic considerations (Cheng et al., 2025). These men may have total testosterone levels appearing within the normal range while still experiencing clinical symptoms of testosterone deficiency and impaired semen quality. Assessment of free testosterone provides greater diagnostic accuracy than total testosterone alone, particularly in men with elevated sex hormone-binding globulin (SHBG) levels (Facondo et al., 2022).

2.5.5 Secondary Hypogonadism and Erectile Dysfunction

Hypogonadism frequently manifests with erectile dysfunction (ED), which itself reflects vascular and endothelial dysfunction. The strong correlation between testosterone levels and erectile function has been well-documented in multiple studies. Men with more severe testosterone deficiency exhibit proportionally worse erectile function on standardized scales (Rehman et al., 2025).

2.5.6 Hyperprolactinemia and Reproductive Dysfunction

Hyperprolactinemia represents an important but often underdiagnosed cause of male hypogonadism and sexual dysfunction. Elevated prolactin levels suppress GnRH secretion through dopaminergic antagonism, thereby reducing FSH and LH secretion and subsequently decreasing testosterone production (Broul, 2025). Men with hyperprolactinemia commonly present with low libido, erectile dysfunction, gynecomastia, and reduced testicular size. Importantly, a rare subset of hyperprolactinemic men present with normal testosterone levels but still exhibit clinical hypogonadal symptoms (Cheng et al., 2025). The prevalence of hyperprolactinemia in men with erectile dysfunction is approximately 2%, but when severe hyperprolactinemia (PRL > 35 ng/mL) is considered, the association becomes more clinically significant (Corona et al., 2024). Treatment with dopamine agonists (bromocriptine or cabergoline) effectively normalizes prolactin levels and, in most cases, substantially improves sexual function and semen quality.

Table 3.

Semen Parameter	Normal Reference	Hypothyroidism	Hyperthyroidism	Primary Hypogonadism	Secondary Hypogonadism
Sperm Concentration (million/mL)	≥15 (Dutta et al., 2019)	8-11 (↓30-45%) (Sengupta & Dutta, 2018)	10-12 (↓20-35%) (Sengupta & Dutta, 2018)	<5 (↓>90%) (Iacobucci et al., 2024)	5-10 (↓30-70%) (Iacobucci et al., 2024)
Total Sperm Count (million)	≥39 (Dutta et al., 2019)	25-37 (↓35-50%) (Sengupta & Dutta, 2018)	23-40 (↓25-40%) (Sengupta & Dutta, 2018)	<20 (↓>95%) (Iacobucci et al., 2024)	10-30 (↓35-75%) (Iacobucci et al., 2024)
Total Sperm Motility (%)	≥40 (Dutta et al., 2019)	24-30 (↓25-40%) (Sengupta & Dutta, 2018)	28-32 (↓20-30%) (Sengupta & Dutta, 2018)	<20 (↓>60%) (Iacobucci et al., 2024)	20-35 (↓20-40%) (Iacobucci et al., 2024)
Progressive Motility (%)	≥32 (Dutta et al., 2019)	20-26 (↓20-35%) (Sengupta & Dutta, 2018)	24-27 (↓15-25%) (Sengupta & Dutta, 2018)	<15 (↓>70%) (Iacobucci et al., 2024)	15-25 (↓20-35%) (Iacobucci et al., 2024)

Sperm Viability (%)	≥54 (Dutta et al., 2019)	43-49 (↓10-20%) (Sengupta & Dutta, 2018)	46-50 (↓10-15%) (Sengupta & Dutta, 2018)	<40 (↓>35%) (Farkouh et al., 2022)	40-55 (↓10-25%) (Iacobucci et al., 2024)
Normal Morphology (%)	≥4 (Dutta et al., 2019)	2.5-3.5 (↓15-25%) (Sengupta & Dutta, 2018)	3.0-3.8 (↓10-20%) (Sengupta & Dutta, 2018)	<2 (↓>90%) (Iacobucci et al., 2024)	3-8 (↓25-50%) (Iacobucci et al., 2024)
Semen Volume (mL)	1.4-7.6 (Dutta et al., 2019)	1.2-5.0 (Sengupta & Dutta, 2018)	1.5-7.0 (Sengupta & Dutta, 2018)	Normal to decreased (Iacobucci et al., 2024)	Normal to decreased (Iacobucci et al., 2024)
DNA Fragmentation Index (%)	<15 (Farkouh et al., 2022)	18-25 (Sengupta & Dutta, 2018)	20-30 (Sengupta & Dutta, 2018)	>30 (>100% increase) (Farkouh et al., 2022)	20-30 (Iacobucci et al., 2024)
Testicular Volume (mL/testis)	15-25 (Dutta et al., 2019)	Normal to reduced (Sengupta & Dutta, 2018)	Normal (Sengupta & Dutta, 2018)	<12 (Atrophic) (Iacobucci et al., 2024)	12-20 (Normal-↓) (Iacobucci et al., 2024)

Table 3 portrays semen quality parameters across endocrine disorders

3. Impact of Pharmacotherapy on Semen Quality

Table 4.

Drug Category	**Specific Drug/Class**	**Effect on Sperm Concentration**	**Effect on Sperm Motility**	**Effect on Morphology**	**Overall Effect**	**Reversibility**	**Clinical Recommendation**	**Key Sources**
Antidepressants	SSRIs (fluoxetin, paroxetine)	Decreased	Decreased	Abnormalities	Negative	Partially reversible	Caution; consider alternatives	(Santos et al., 2025)
	Other Antidepressants (trazodone, lithium)	Decreased	Decreased	Increased abnormalities	Negative	Partially reversible	Caution; monitor fertility	(Santos et al., 2025)
	Mirtazapine	Decreased/ Mixed	Decreased	Mixed effects	Negative	Partially reversible	May have advantages over others	(Santos et al., 2025)
Antiretroviral Drugs	Dolutegravir, Tenofovir, Emtricitabine	Decreased/ Altered kinematics	Decreased	Altered	Negative	Effects persist	Monitor if using PrEP/HIV treatment	(Pinto & Aneck-Hahn, 2025)

	Abacavir, Etravirine	Sperm DNA damage increased	Not significantly altered	Potential damage	Negative	Potential DNA damage	Monitor spermatogenesis	(Matuszewska et al., 2021)
Statins	Atorvastatin	Decreased (-31%)	Altered morphology/motility changes	Abnormalities (head, neck, midpiece)	Negative	May persist post-treatment	Consider alternative; monitor parameters	(Pons-Rejraji et al., 2014)
GLP-1 Receptor Agonists	Liraglutide, Semaglutide	Increased (obese men only)	Improved (obese men)	Improved (obese men)	Positive (metabolic dysfunction)	Reversible with cessation	May benefit obese hypogonadal men	(Deameh et al., 2025)
	In healthy men	No effect	No effect	No effect	Neutral	N/A	No contraindication in healthy men	(Service et al., 2023)
Anabolic-Androgenic Steroids	AAS (testosterone abuse)	Similar but motility ↓	Lower in users	Similar to controls	Negative	Partially reversible	CONTRAINDICATED for fertility	(Mulawkar et al., 2023)
Testosterone Replacement (Traditional)	High-dose TRT	Severe decrease/Azoospermia	Severely impaired	Severely affected	Severely Negative	Recovery: 8+ months, may be incomplete	CONTRAINDICATED for fertility-seeking men	(Song et al., 2019)
Testosterone Replacement (Intranasal)	Natesto (pulsatile)	Maintained /Preserved	Maintained	Maintained	Positive (fertility-preserving)	N/A (preserving)	Preferred for fertility preservation	(Ramasamy et al., 2020)
Testosterone Replacement (Oral)	Oral testosterone undecanoate	No significant change	No significant change	No significant change	Positive (fertility-preserving)	N/A (fertility-preserving)	Preferred for fertility preservation	(Saffati et al., 2024)
Gonadotropins (hCG/FSH)	hCG + rFSH combination	Increased (85.7% with sperm)	Improved	Improved	Positive	N/A (therapeutic)	GOLD STANDARD for fertility preservation	(Orta et al., 2019)

Table 4 presents Impact of Pharmacotherpahy on Semen Quality.

SSRIs - Selective Serotonin Reuptake Inhibitors, PrEP/HIV- Pre-exposure prophylaxis/Human Immunodeficiency Virus, DNA - Deoxyribonucleic acid, GLP-1 - Glucagon-Like Peptide-1, N/A - not applicable, AAS - Anabolic-Androgenic Steroids, HRT - Hormone Replacement Therapy, hCG/FSH - Human Chorionic Gonadotropin/Follicle-Stimulating Hormone, hCG + rFSH - Human Chorionic Gonadotropin and recombinant Follicle-Stimulating Hormone, % - percent

4. Clinical Implications and Future Directions

The mounting evidence linking common chronic diseases to impaired male reproductive function necessitates a fundamental shift in clinical practice toward recognizing infertility as a systemic manifestation of underlying pathology. Clinicians should integrate reproductive health assessment into routine management of patients with metabolic, cardiovascular, autoimmune, endocrine, and renal diseases, as male infertility increasingly serves as a harbinger of occult systemic disease. For patients with type 2 diabetes mellitus, aggressive glycemic control represents a critical intervention, as studies demonstrate substantial improvements in semen parameters when metabolic dysfunction is optimized (Sm et al., 2025; R et al., 2026). Similarly, weight reduction strategies in obese men have shown significant promise in restoring semen quality and fertility potential (Service et al., 2023), with emerging evidence suggesting that GLP-1 receptor agonists may offer additional reproductive benefits in metabolically compromised men (Deameh et al., 2025). In patients with hypertension and cardiovascular disease, blood pressure optimization and vascular risk factor modification should be prioritized as fertility-preserving interventions (Colli et al., 2019). For men with autoimmune conditions, particularly those requiring immunomodulatory therapy, careful medication selection is essential, as biologic agents such as TNF inhibitors demonstrate superior reproductive safety profiles compared to conventional disease-modifying antirheumatic drugs (Finelli et al., 2021; Ma et al., 2024). Notably, patients with chronic kidney disease represent a population where reproductive function may be partially recoverable; kidney transplantation has been shown to improve erectile function and normalize spermatogenesis in previously azoospermic men (Nguyen et al., 2025). Regarding pharmacotherapy, clinicians must exercise caution with medications known to compromise fertility, including selective serotonin reuptake inhibitors (Santos et al., 2025) and high-dose testosterone replacement therapy (Song et al., 2019), while preferentially recommending fertility-preserving alternatives such as intranasal testosterone formulations (Ramasamy et al., 2020) or gonadotropin-based therapy (Orta et al., 2019) for hypogonadal men desiring paternity. Future research should establish standardized screening protocols incorporating semen analysis into the diagnostic workup of men with chronic diseases, develop targeted multimodal interventions addressing both primary pathology and reproductive dysfunction, and conduct longitudinal studies examining the impact of disease optimization on fertility outcomes and quality of life. Additionally, mechanistic investigations elucidating the precise molecular pathways linking systemic inflammation, oxidative stress, and hormonal dysregulation to testicular dysfunction will inform the development of novel therapeutics capable of restoring reproductive capacity in this vulnerable population.

5. Conclusions

The synthesis of current research demonstrates that common chronic diseases—specifically obesity, diabetes, cardiovascular disorders, and autoimmune conditions—exert a profound and multifaceted negative impact on male reproductive health. The impairment of semen quality is not a localized phenomenon but rather a systemic consequence of interconnected pathomechanisms. Key drivers include heightened oxidative stress, chronic low-grade systemic inflammation, and the disruption of the hypothalamic-pituitary-gonadal (HPG) axis. Furthermore, microvascular endothelial dysfunction and direct metabolic interference with spermatogenesis lead to significant reductions in sperm concentration, motility, and morphological integrity. Crucially, the degree of semen quality deterioration often correlates with the severity and duration of the chronic condition. This underscores the necessity for a multidisciplinary approach to male infertility, where managing the underlying systemic disease is as vital as direct fertility treatments. Early clinical intervention, lifestyle modifications, and targeted antioxidant therapies may mitigate these adverse effects. Ultimately, preserving male reproductive potential requires a comprehensive understanding of how systemic health dictates testicular function, highlighting the importance of including semen analysis as a diagnostic consideration in the long-term management of men with chronic illnesses.

Disclosure

Funding: This research received no external funding.

Author Contributions:

All authors contributed to the article.

All authors have read and agreed with the published version of the manuscript.

Conceptualization: Wiktor Śliwiński

Methodology: Daniel Chołuj, Karolina Zarówna

Check: Wiktor Śliwiński, Weronika Pura

Formal analysis: Mateusz Kosowski

Writing – rough preparation, review and editing: Dominika Matecka, Jakub Mazur, Daniel Chołuj, Weronika Pura, Karolina Zarówna, Mateusz Kosowski, Wiktor Śliwiński, Jakub Marciniak

Supervision: Dominika Matecka

Project administration: Jakub Mazur

Conflict of Interest Statement: The authors report no conflict of interest.

Financial Disclosure: The study did not receive any funding.

AI: AI was utilized for assistance in refining the academic English language of the manuscript, ensuring clarity, consistency, and adherence to scientific writing standards. It is important to emphasize that all AI tools were used strictly as assistive instruments under human supervision. The final interpretation of results, classification of errors, and conclusions were determined by human experts in clinical medicine and formal logic. In preparing this work, the author(s) used Grammarly for the purpose of checking and improving grammatical correctness. After using this tool, the author(s) have reviewed and edited the content as needed and accept full responsibility for the substantive content of the publication.

REFERENCES

1. Wang, Y., Fu, X., & Li, H. (2025). Mechanisms of oxidative stress-induced sperm dysfunction. *Frontiers in Endocrinology*. https://doi.org/10.3389/fendo.2025.1520835
2. Patan, G. T., Moreira, R. J., Russo, A., Pereira, M. L., Oliveira, P. F., Barreca, D., & Alves, M. (2025). Lifestyle implications of the paradox and management of oxidative stress in sperm. *The Journal of Physiology*. https://doi.org/10.1113/JP289694
3. Nowicka-Bauer, K., & Nixon, B. (2020). Molecular changes induced by oxidative stress that impair human sperm motility. *Antioxidants, 9*(2), 134. https://doi.org/10.3390/antiox9020134
4. Mosanezhad, Z., Abbasihormozi, S., Shokri, M., Hosseini, R., & Sabbaghian, M. (2025). The influence of body mass index on oxidative stress markers in infertile men's semen parameters. *Clinical and Experimental Reproductive Medicine*. https://doi.org/10.5653/cerm.2025.07955
5. Dutta, S., Sengupta, P., Slma, P., & Roychoudhury, S. (2021). Oxidative stress, testicular inflammatory pathways, and male reproduction. *International Journal of Molecular Sciences, 22*(18), 10043. https://doi.org/10.3390/ijms221810043
6. S, B., S., V. A., C, P., D, J., & B, B. (2025). Testicular oxidative stress and antioxidant therapies in male infertility: An evidence-based review. *Benha Medical Journal*. https://doi.org/10.21608/bmfj.2025.400353.2519
7. Fang, Y., Su, Y., Xu, J., Hu, Z., Zhao, K., Liu, C., & Zhang, H. (2021). Varicocele-mediated male infertility: From the perspective of testicular immunity and inflammation. *Frontiers in Immunology*. https://doi.org/10.3389/fimmu.2021.729539
8. Potiris, A., Moustakli, E., Trismpioti, E., Drakaki, E., Mavrogianni, D., Matsas, A., Zikopoulos, A., Sfakianakis, A., Tsakiridis, I., Dagklis, T., Zachariou, A., Christopoulos, P., Domali, E., Drakakis, P., & Stavros, S. (2025). From inflammation to infertility: How oxidative stress and infections disrupt male reproductive health. *Metabolites*. https://doi.org/10.3390/metabo15040267
9. Guazzone, V., Jacobo, P., Theas, M., & Lustig, L. (2009). Cytokines and chemokines in testicular inflammation: A brief review. *Microscopy Research and Technique, 72*(8), 620–628. https://doi.org/10.1002/jemt.20704
10. Li, N., Wang, T., & Han, D. (2012). Structural, cellular and molecular aspects of immune privilege in the testis. *Frontiers in Immunology, 3*, 152. https://doi.org/10.3389/fimmu.2012.00152
11. Elmas, M., Ozakpinar, O., Kolgazi, M., Ener, G., Arbak, S., & Ercan, F. (2022). Exercise improves testicular morphology and oxidative stress parameters in rats with testicular damage induced by a high-fat diet. *Andrologia*. https://doi.org/10.1111/and.14600

12. Loveland, K. L., Klein, B., Pueschl, D., Indumathy, S., Bergmann, M., Loveland, B. E., Hedger, M. P., & Schuppe, H.-C. (2017). Cytokines in male fertility and reproductive pathologies: Immunoregulation and beyond. *Frontiers in Endocrinology, 8*, 307. https://doi.org/10.3389/fendo.2017.00307
13. Corona, G., Goulis, D., & Liu, P. Y. (2023). The biochemical confirmation of adult male hypogonadism: Global perspectives from the International Society of Andrology. *Clinical Endocrinology*. https://doi.org/10.1111/cen.14941
14. Jaramillo, L. D., Hill, J. W., Smedlund, K., & Manaserh, I. H. (2025). Astrocyte insulin-like peptide signaling and control of murine sexual maturation/function. *Journal of the Endocrine Society*. https://doi.org/10.1210/jendso/bvaf149.1509
15. Elias, C. F., & Purohit, D. (2012). Leptin signaling and circuits in puberty and fertility. *Cellular and Molecular Life Sciences, 70*, 841–862. https://doi.org/10.1007/s00018-012-1095-1
16. Rabijewski, M. (2023). Male-specific consequences of obesity: Functional hypogonadism and fertility disorders. *Endokrynologia Polska*. https://doi.org/10.5603/ep.95626
17. Mahmood, A., Steinberg, B., Chang, J., Bourricaudy, R. A., Bhutani, S., Varela, J., & Campbell, K. (2025). GLP-1 agonists and testosterone deficiency: A systematic review of clinical and preclinical evidence. *The Journal of Sexual Medicine*. https://doi.org/10.1093/jsxmed/qdaf320.268
18. Huang, R., Chen, J., Guo, B., Jiang, C., & Sun, W. (2024). Diabetes-induced male infertility: Potential mechanisms and treatment options. *Cell & Bioscience, 14*, Article 13. https://doi.org/10.1186/s10020-023-00771-x
19. Ye, L., Huang, W., Liu, S., Cai, S., Hong, L., Xiao, W., Thiele, K., Zeng, Y., Song, M., & Diao, L. (2021). Impacts of immunometabolism on male reproduction. *Frontiers in Immunology, 12*, 658432. https://doi.org/10.3389/fimmu.2021.658432
20. Gabriel, A. L. R., Fioretto, M. N., Barata, L. A., Justulin, L. A., & Felisbino, S. (2025). Metabolic insights into male fertility: A narrative review of the role of adiponectin on the hypothalamic-pituitary-testicular axis. *Biology of Reproduction*. https://doi.org/10.1093/biolre/ioaf266
21. Pandian, K., Huang, L., Junaid, A., Harms, A. C., van Zonneveld, A., & Hankemeier, T. (2024). Tracer-based metabolomics for profiling nitric oxide metabolites in a 3D microvessels-on-chip model. *The FASEB Journal*. https://doi.org/10.1096/fj.202400553R
22. Kwaifa, I., & Noor, S. (2024). Modulatory potentials of nitric oxide in obesity-induced endothelial dysfunction. *Edelweiss Applied Science and Technology*. https://doi.org/10.55214/25768484.v8i6.2730
23. Penna, C., & Pagliaro, P. (2025). Endothelial dysfunction: Redox imbalance, NLRP3 inflammasome, and inflammatory responses in cardiovascular diseases. *Antioxidants*. https://doi.org/10.3390/antiox14030256
24. Virdis, A., Colucci, R., Bernardini, N., Blandizzi, C., Taddei, S., & Masi, S. (2018). Microvascular endothelial dysfunction in human obesity: Role of TNF-α. *The Journal of Clinical Endocrinology & Metabolism*. https://doi.org/10.1210/jc.2018-00512
25. Lai, P., Jing, Y., Guo, L., Qin, T., Xue, Y., Zhang, Z., Wang, X., Miao, X., Zhang, W., & Ding, G. (2022). Abscopal effects of thoracic X-ray radiation on spermatogenesis in mice. *Frontiers in Physiology*. https://doi.org/10.3389/fphys.2022.984429
26. Aleksandrowicz, M., Konop, M., Rybka, M., Mazurek, U., Stradczuk-Mazurek, M., Kciuk, M., Bdzyska, B., Dobrowolski, L., & Kuczeriszka, M. (2025). Dysfunction of microcirculation in atherosclerosis: Implications of nitric oxide, oxidative stress, and inflammation. *International Journal of Molecular Sciences*. https://doi.org/10.3390/ijms26136467
27. Donato, A., Pierce, G., Lesniewski, L., & Seals, D. (2009). Role of NF-κB in age-related vascular endothelial dysfunction in humans. *Aging*. https://doi.org/10.18632/AGING.100080
28. Sm, D., Ao, A., K, M., Bc, L., & Cs, O. (2025). The impact of diabetes mellitus-related oxidative stress on male fertility: A review. https://doi.org/10.1111/1753-0407.70157
29. R, W., Y, Z., H, L., W, L., L, X., & M, L. (2026). Effect of type 2 diabetes mellitus on sperm quality and outcomes of assisted reproductive techniques in infertile male patients. *Frontiers in Endocrinology*. https://doi.org/10.3389/fendo.2025.1692746
30. A, A., Mm, A., & M, H. (2025). Diabetes and male infertility: A review of sperm chromatin damage and epigenetic effects. *International Journal of Reproductive BioMedicine*. https://doi.org/10.18502/ijrm.v23i10.20312
31. Eo, N., Y, L., H, Z., B, X., Q, L., Mi, Z., & J, X. (2025). Potential role of 4-hydroxyisoleucine in enhancing fertility in male mice with diet-induced obesity. *Frontiers in Endocrinology*. https://doi.org/10.3389/fendo.2025.1561543
32. D, M., M, Z., X, Z., & L, X. (2025). Beyond body mass index: The role of fat distribution in male sperm quality. *Frontiers in Endocrinology*. https://doi.org/10.3389/fendo.2025.1702791
33. R, F., D, C., W, Z., J, Z., S, C., & Y, X. (2025). Immune microenvironment dysregulation: A contributing factor to obesity-associated male infertility. *Biomedicines*. https://doi.org/10.3390/biomedicines13061314
34. K, L., W, N., H, H., Y, W., J, W., L, Y., G, H., Z, T., J, Y., P, H., L, H., X, C., X, W., & X, L. (2025). Nicotinamide mononucleotide treatment improves spermatogenesis in obese mice by reducing lysine acetylation of lactate dehydrogenase C. *Communications Biology*. https://doi.org/10.1038/s42003-025-09094-5

35. D, M., & J, X. (2025). Correlation study and full management of metabolic syndrome and sperm DNA fragmentation index, a regional multicentre prospective long-term follow-up study from Anhui, China. *Frontiers in Cell and Developmental Biology*. https://doi.org/10.3389/fcell.2025.1586069
36. J, Z., S, H., Y, O., Y, K., & M, L. (2025). Immunometabolism and male reproductive function: Linking inflammation, oxidative stress, and declining fertility. *Frontiers in Immunology*. https://doi.org/10.3389/fimmu.2025.1736492
37. Colli, L. G., Belardin, L. B., Echem, C., Akamine, E. H., Antoniassi, M. P., Andretta, R. R., Mathias, L. S., Rodrigues, S. F. P., Bertolla, R. P., & de Carvalho, M. H. C. (2019). Systemic arterial hypertension leads to decreased semen quality and alterations in the testicular microcirculation in rats. *Scientific Reports, 9*(1), 11047. https://doi.org/10.1038/s41598-019-47157-w
38. Costa, J., Braga, P. C., Rebelo, I., Oliveira, P. F., & Alves, M. G. (2023). Mitochondria quality control and male fertility. *Biology, 12*(6), 827. https://doi.org/10.3390/biology12060827
39. Kaltsas, A., Koumenis, A., Stavropoulos, M., Kratiras, Z., Deligiannis, D., Adamos, K., & Chrisofos, M. (2025). Male infertility and reduced life expectancy: Epidemiology, mechanisms, and clinical implications. *Journal of Clinical Medicine, 14*(11), 3930. https://doi.org/10.3390/jcm14113930
40. Martins da Silva, S., & Anderson, R. A. (2022). Reproductive axis ageing and fertility in men. *Reviews in Endocrine and Metabolic Disorders, 23*(6), 1109–1121. https://doi.org/10.1007/s11154-022-09759-0
41. Hart, R. (2023). Environmental exposures: Impact on male fertility. *Fertility & Reproduction*. https://doi.org/10.1142/S2661318223740699
42. Finelli, R., Leisegang, K., Finocchi, F., De Masi, S., Agarwal, A., & Damiani, G. (2021). The impact of autoimmune systemic inflammation and associated medications on male reproductive health in patients with chronic rheumatological, dermatological, and gastroenterological diseases: A systematic review. *American Journal of Reproductive Immunology, 85*(5), e13389. https://doi.org/10.1111/aji.13389
43. Fendereski, K., Horns, J., Dehghanbanadaki, H., Schardein, J., Jimbo, M., Gross, K., Pastuszak, A., & Hotaling, J. (2024). The association between sperm quality and urological and medical comorbidities. *The Journal of Sexual Medicine, 21*(Suppl. 7), qdae167.193. https://doi.org/10.1093/jsxmed/qdae167.193
44. Scriffignano, S., Perrotta, F., & Lubrano, E. (2024). Male fertility in spondyloarthritis: From clinical issues to cytokines milieu. A narrative review. *Andrology*. https://doi.org/10.1111/andr.13772
45. Aziz, A., Hussain, S., Ali, W., Haq, E. ul, Asghar, R., Khan, T., Aziz, P. A., Rawalpindi, & Pakistan. (2025). Comparison of impaired fertility in men newly diagnosed with rheumatoid arthritis with general population. *First Workshop on Insights from Negative Results in NLP*. https://doi.org/10.71000/a8hn9x71
46. Zhu, J., Zhu, Q., Li, X., Shen, T., Shi, X., & Zhao, T. (2025). Systemic lupus erythematosus and male reproductive health: A systematic review and meta-analysis. *Autoimmunity Reviews, 24*(4), 103742. https://doi.org/10.1016/j.autrev.2025.103742
47. Waters, T. H. B., Chan, C. P. S., Li, T. C., & Chan, D. Y. L. (2020). Influence of the period of abstinence on semen quality in a patient with systemic lupus erythematosus: A case report and review of the literature. *Case Reports in Rheumatology, 2020*, 9296858. https://doi.org/10.1155/2020/9296858
48. Keskin, H., & Altan, M. (2025). Male infertility and erectile dysfunction in patients with vasculitis. *Acta Medica*. https://doi.org/10.32552/2025.ActaMedica.1229
49. Elhanbly, S., Shendy, D., & Zohdy, M. (2025). Effect of methotrexate on semen parameters in psoriatic male patients. *Cureus, 17*(6), e85787. https://doi.org/10.7759/cureus.85787
50. Scott, M., Rodriguez, A., Marciano, O., Lundy, S., & Raheem, O. (2024). The impact of environmental factors and chronic medical conditions on semen qualities: A ten-year longitudinal analysis. *The Journal of Sexual Medicine*. https://doi.org/10.1093/jsxmed/qdae167.121
51. Lehtihet, M., & Hylander, B. (2015). Semen quality in men with chronic kidney disease and its correlation with chronic kidney disease stages. *Andrologia*. https://doi.org/10.1111/and.12388
52. Kariev, S. S., Nasirov, F. R., Shavakh, S. S., & Ibadov, E. R. (2026). Erectile function and reproductive health in men with chronic kidney disease receiving renal replacement therapy. *Urology Herald*. https://doi.org/10.21886/2308-6424-2025-13-6-16-26
53. Eckersten, D., Tsatsanis, C., Giwercman, A., Bruun, L., Pihlsgrd, M., & Christensson, A. (2017). MicroRNA-155 and anti-Müllerian hormone: New potential markers of subfertility in men with chronic kidney disease. *Nephron Extra*. https://doi.org/10.1159/000458711
54. Nguyen, N. T., Nguyen, H. H. Q., Takeshima, T., Kuroda, S., Yumura, Y., Atmoko, W., & Nguyen, H. D. K. (2025). Natural pregnancy following kidney transplantation in an azoospermic male: A case report. *Translational Andrology and Urology*. https://doi.org/10.21037/tau-2025-319
55. Kim, M., Kim, S., Rou, W., Hwang, S., & Lee, B. (2015). Erectile dysfunction in patients with liver disease related to chronic hepatitis B. *Clinical and Molecular Hepatology*. https://doi.org/10.3350/cmh.2015.21.4.352
56. Ali, R. A., Awadalla, E. A., Amin, Y., Fouad, S. S., Ahmed, M. A.-E. B., Hassan, M. H., Abdel-kahaar, E., & Abdel-Aziz, R. H. (2024). The deleterious effects of sofosbuvir and ribavirin (antiviral drugs against hepatitis C virus) on different body systems in male albino rats regarding reproductive, hematological, biochemical, hepatic, and renal profiles and histopathological changes. *Scientific Reports*. https://doi.org/10.1038/s41598-024-55950-5

57. Dutta, S., Sengupta, P., & Muhamad, S. (2019). Male reproductive hormones and semen quality. *Asian Pacific Journal of Reproduction*. https://doi.org/10.4103/2305-0500.268132
58. Sengupta, P., & Dutta, S. (2018). Thyroid disorders and semen quality. https://doi.org/10.13005/bpj/1342
59. Cheng, X., Xiao, Y., Deng, Y., Chen, Q., Wen, X., Zhou, E., & Zhou, H. (2025). Idiopathic hyperprolactinemia-associated hypogonadism in men presenting with normal testosterone levels. *PLoS ONE*. https://doi.org/10.1371/journal.pone.0332871
60. Facondo, P., Lodovico, E. D., Pezzaioli, L., Cappelli, C., Ferlin, A., & Delbarba, A. (2022). Usefulness of routine assessment of free testosterone for the diagnosis of functional male hypogonadism. *The Aging Male*. https://doi.org/10.1080/13685538.2022.2046727
61. Rehman, K. U., Manan, F., & Jan, M. A. (2025). Correlation between serum testosterone levels and erectile dysfunction severity in Pakistani men aged 40–65 years. *Cureus*. https://doi.org/10.7759/cureus.93449
62. Broul, M. (2025). Prolactin hypersecretion and its association with erectile dysfunction. *The Journal of Sexual Medicine*. https://doi.org/10.1093/jsxmed/qdaf077.148
63. Corona, D. G., Rastrelli, G., Bianchi, N. D., Sparano, C. D., Sforza, A. D., Vignozzi, L., & Maggi, M. (2024). Hyperprolactinemia and male sexual function: Focus on erectile dysfunction and sexual desire. *The Journal of Sexual Medicine*. https://doi.org/10.1093/jsxmed/qdae041.036
64. Iacobucci, A., Naeem, T., Saffati, G., Gadiwalla, Q., Mody-Bailey, N., Green, C., Lipshultz, L., & Khera, M. (2024). Testosterone replacement therapy in hypogonadism: A single center longitudinal analysis of treatment patterns and clinical outcomes. *The Journal of Sexual Medicine*. https://doi.org/10.1093/jsxmed/qdae001.315
65. Farkouh, A., Salvio, G., Kuroda, S., Saleh, R., Vogiatzi, P., & Agarwal, A. (2022). Sperm DNA integrity and male infertility: A narrative review and guide for the reproductive physicians. *Translational Andrology and Urology*. https://doi.org/10.21037/tau-22-149
66. Santos, L. O. D. P. D., Silva, P. R. Q. D., Rigo, G. M. O., Pinto, C. L. O., Perini, H. F., & Siervo, G. E. M. L. (2025). Can antidepressants compromise sperm quality? A comprehensive review of preclinical evidence. *Sexual Medicine Reviews*. https://doi.org/10.1093/sxmrev/qeaf056
67. Pinto, S. Z., & Aneck-Hahn, N. (2025). Effect of in vitro exposure of first-line antiretrovirals on healthy human spermatozoa on kinematics and motility. *International Urology and Nephrology*. https://doi.org/10.1007/s11255-024-04340-x
68. Matuszewska, A., Nowak, B., Niaski, W., Eberhardt, M., Domrazek, K., Nikodem, A., Wiatrak, B., Zduniak, K., Olejnik, K., Merwid-Ląd, A., Tomkalski, T., Jędrzejuk, D., Szeląg, E., Podhorska-Okolów, M., Piotrowska, A., Jękowiak, I., Heinrich, A., Rutkowska, M., Dziewiszek, W., ... Szeląg, A. (2021). Long-term administration of abacavir and etravirine impairs semen quality and alters redox system and bone metabolism in growing male Wistar rats. *Oxidative Medicine and Cellular Longevity, 2021*, 5596090. https://doi.org/10.1155/2021/5596090
69. Pons-Rejraji, H., Brugnon, F., Sion, B., Maqdasy, S., Gouby, G., Pereira, B., Marceau, G., Gremeau, A., Drevet, J., Grizard, G., Janny, L., & Tauveron, I. (2014). Evaluation of atorvastatin efficacy and toxicity on spermatozoa, accessory glands and gonadal hormones of healthy men: A pilot prospective clinical trial. *Reproductive Biology and Endocrinology, 12*, 65. https://doi.org/10.1186/1477-7827-12-65
70. Deameh, M., Raheem, O., Ramez, M., Rowaiee, R., Irshid, B. A. B., Mohamed, H., Mohamed, T., Abdelshafi, A., & Al-Osoufi, M. A. (2025). Effects of GLP-1 receptor agonists on male reproductive hormones, semen parameters, and metabolic outcomes: A systematic review. *The Journal of Sexual Medicine*. https://doi.org/10.1093/jsxmed/qdaf320.152
71. Service, C. A., Puri, D., Azzawi, S. A., Hsieh, T.-C., & Patel, D. P. (2023). The impact of obesity and metabolic health on male fertility: A systematic review. *Fertility and Sterility*. https://doi.org/10.1016/j.fertnstert.2023.10.017
72. Mulawkar, P., Maheshwari, P., Gauhar, V., Agrawal, S., Mohammed, T. O., Singh, A. G., Tak, G. R., Shah, U., Shukla, D., & Mamankar, D. (2023). Use of anabolic-androgenic steroids and male fertility: A systematic review and meta-analysis. *Journal of Human Reproductive Sciences*. https://doi.org/10.4103/jhrs.jhrs_90_23
73. Song, S., Sung, S., Her, Y., Oh, M., Shin, D., Lee, J., Baek, J., Lee, W., & Kim, D. S. (2019). Misuse of testosterone replacement therapy in men in infertile couples and its influence on infertility treatment. *Clinical and Experimental Reproductive Medicine*. https://doi.org/10.5653/cerm.2019.00290
74. Ramasamy, R., Masterson, T. A., Best, J. C., Bitran, J., Ibrahim, E., Molina, M., Kaiser, U. B., Miao, F., & Reis, I. M. (2020). Effect of Natesto on reproductive hormones, semen parameters and hypogonadal symptoms: A single center, open label, single arm trial. *The Journal of Urology*. https://doi.org/10.1097/JU.0000000000001078
75. Saffati, G., Rendon, D. O., Kronstedt, S., Hinojosa-Gonzalez, D., & Khera, M. (2024). Effects of oral testosterone undecanoate on semen parameters in hypogonadal men: An interim analysis of a prospective pilot study. *The Journal of Sexual Medicine*. https://doi.org/10.1093/jsxmed/qdae167.065
76. Orta, M., Hıdır, M., Salaba, E., Boyuk, A., Beşe, C., Pazır, Y., & Kadıoğlu, A. (2019). Evaluation of gonadotropin-replacement therapy in male patients with hypogonadotropic hypogonadism. *Asian Journal of Andrology*. https://doi.org/10.4103/aja.aja_6_19
77. Deameh, M. G., Ramez, M., Rowaiee, R., Bani Irshid, B. A., Mohamed, H., Abdelshafi, A., Al-Osoufi, M. A., Mohamed, T., Hegazin, S. B., & Raheem, O. (2026). Effects of glucagon-like peptide-1 receptor agonists on male reproductive hormones, semen parameters, and metabolic outcomes: A systematic review. *The Journal of Sexual Medicine, 23*(2), qdaf381. https://doi.org/10.1093/jsxmed/qdaf381