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Infection of *Toxoplasma gondii* in men leads to decapitation of sperms: a concern on male infertility

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ABSTRACT:

Toxoplasma gondii is a widespread protozoan parasite capable of infecting nearly all warm-blooded animals, including humans. Although often asymptomatic, infection has been increasingly associated with reproductive complications, particularly in men. Evidence suggests that the parasite may impair male fertility through multiple pathways, including disruption of the blood–testis barrier, direct interaction with sperm, and induction of oxidative stress and inflammatory responses. Hormonal alterations, especially in testosterone regulation, have also been reported, though findings are inconsistent. Clinical and experimental studies further indicate possible effects on semen parameters, including sperm morphology. However, data remain fragmented, and results across populations and models are not always consistent. In addition, currently available therapeutic strategies are not tailored to mitigate reproductive outcomes and may themselves compromise fertility. This review brings together existing findings on the potential links between *T. gondii* infection and male infertility, while emphasizing that the mechanisms and clinical relevance of these associations are not yet fully understood. Further studies are required to determine causality, define underlying biological pathways, and understand the implications for male reproductive health.

Keywords: *Toxoplasma gondii*, Male infertility, Sperm damage, Oxidative stress, Testosterone.

INTRODUCTION

Toxoplasma gondii is an obligate intracellular protozoan parasite capable of infecting nearly all warm-blooded animals, including humans, as intermediate hosts[1]. Global seroprevalence varies considerably as it is influenced by environmental conditions, hygiene practices and dietary habits. Lower prevalence is reported in Southeast Asia, China, Korea, and colder regions such as Scandinavia, where infection rates range from 4% to 39%. In contrast, higher prevalence has been recorded in West African countries (54-77%) and several Latin American nations (51-72%)[2].

It is estimated that one-third of the world's population carries the parasite. Most infections remain asymptomatic and progress to a chronic state[1], but in immunocompromised individuals, acute infections can be life-threatening, and latent infections may reactivate as immune function declines[3].

Following ingestion, the parasite proliferates rapidly as tachyzoites during the acute phase and disseminates throughout the host, ultimately localizing in various organs, including the reproductive system[1]. Growing evidence suggests that infection with *T. gondii* may impair male reproductive health. The parasite has been detected in semen[4] and has been linked to disturbances of the hypothalamic-pituitary-gonadal axis, which may cause testicular damage or secondary hypogonadism[5]. Animal studies report decreased sperm motility and viability, higher rates of abnormal morphology[6], and pathological changes in the testes, epididymis, and prostate[7].

Additionally, *T. gondii* infection induces oxidative stress and apoptosis, which can damage sperm chromatin and DNA, both of which are critical for fertility[8]. *In vitro* studies[9] further show that tachyzoites can directly interact with human spermatozoa, producing a considerable proportion of headless sperm. This striking observation suggests that infection with *T. gondii* may be associated with male sterility.

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LIFECYCLE OF *T. GONDII*

Felines, particularly domestic cats, are the only known definitive hosts of *T. gondii*. They shed unsporulated oocysts in their feces, typically for 1-3 weeks, in large quantities. These oocysts become infective after sporulating in the environment within 1-5 days. Intermediate hosts, including birds, rodents, livestock, and humans, acquire the infection by ingesting sporulated oocysts through contaminated soil, water, food, or vegetation. Once inside the host, oocysts release tachyzoites, which proliferate rapidly and disseminate throughout the body, initiating the acute phase of toxoplasmosis. Over time, tachyzoites differentiate into slow-replicating bradyzoites that form tissue cysts. These cysts develop primarily in neural and muscular tissues such as the brain and skeletal muscles, but they may also be found in the lungs, eyes, and other organs. After its establishment, these cysts can persist for the lifetime of the host[1,9,10].

TRANSMISSION ROUTES OF *T. GONDII*

Transmission most commonly occurs through ingestion of undercooked meat that contains tissue cysts, enabling horizontal transmission among intermediate hosts. Cats typically acquire the infection by consuming infected prey that harbors tissue cysts, which completes and reinforces the parasite's lifecycle. Vertical transmission from mother to fetus is also possible, and in rare cases, the parasite can spread through blood transfusion or organ transplantation[1,10].

Growing evidence from animal studies suggests that *T. gondii* may also be transmitted sexually. In rats, the parasite has been shown to breach the blood–testis barrier (BTB) from the epithelium to the seminiferous tubules, bypassing Sertoli cell defenses. Viable tachyzoites were detected in the ejaculate and were able to infect mated females and their offsprings[9,11,12]. Similar findings have been reported in dogs[13], goats[14] and rabbits[15,16], where viable parasites have been isolated from semen and confirmed to transmit sexually. Experimental insemination of sheep with semen spiked with *T. gondii* has also led to seroconversion[17]. These findings suggest that the parasite can cross the BTB, an anatomical defense that is typically highly resistant to pathogen invasion (Table 1).

More recently, *T. gondii* cysts have been identified in semen samples of immunocompetent men with latent infection[18]. Indirect evidence in humans further supports the possibility of sexual transmission. For instance, an epidemiological study of couples found that male seropositivity was linked to a higher risk of infection in female partners[19]. Additional reports suggest that oral sex may serve as a transmission route, particularly in heterosexual women and men who have sex with men[20].

Clinical Manifestations of *T. gondii* Infection

T. gondii infection is typically asymptomatic. However, 10-20% of individuals with acute infection may experience flu-like symptoms or cervical lymphadenopathy. These cases are usually self-limiting, with symptoms resolving within weeks or months. Occasionally, ocular involvement such as retinochoroiditis may occur, potentially leading to visual impairment[10]. Rarely, testicular toxoplasmosis has also been reported, including a case in a healthy 26-year-old male with chronic granulomatous inflammation of the testes[21].

In immunocompromised individuals, particularly those with acquired immunodeficiency syndrome (AIDS) or those undergoing immunosuppressive therapy, the risk of severe disease is much higher. Reactivation of latent infection is common and can lead to life-threatening complications such as toxoplasmic encephalitis, the most frequent cause of intracerebral mass lesions in AIDS subjects[22]. Other manifestations may include pneumonitis, systemic illness or ocular disease[8].

When primary maternal infection occurs during pregnancy, congenital toxoplasmosis can occur. The risk and severity of fetal infection depend on the gestational age at the time of transmission. Hence, early diagnosis and maternal treatment are essential for reducing both transmission rates and the severity of fetal complications[1]. Although many congenitally infected infants appear asymptomatic at birth, they may later develop neurologic or ocular sequelae[10]. Ocular toxoplasmosis may result from either congenital or postnatally acquired infection. In congenital cases, retinal lesions often manifest in adolescence or adulthood and may cause significant visual loss[1].

EFFECT ON MALE FERTILITY DUE TO *T. GONDII* INFECTION

Several studies suggest that *T. gondii* infection may impair male fertility, although the precise mechanisms remain uncertain[23]. In one study[24] from China, the prevalence of toxoplasmosis was significantly higher among infertile couples (34.83%) compared with fertile controls (12.11%). Infected men also had elevated levels of anti-sperm antibodies. Another study[25] of 200 men confirmed this pattern, reporting a prevalence of 36% among infertile men compared with 11% in fertile counterparts.

More recent work supports these findings. Men with abnormal semen parameters, such as low sperm count, reduced motility, and abnormal morphology, were more likely to test positive for *T. gondii*. In a study[2], adverse semen analysis results were observed in 59.09% of *Toxoplasma*-infected smokers, 46.15% of *Toxoplasma*-infected non-smokers, 43.08% of non-infected smokers, and 43.75% of non-infected non-smokers. Among smokers, the prevalence of toxoplasmosis was notably higher in men with oligozoospermia, asthenozoospermia, and teratozoospermia compared to those with normozoosper-

Table 1 . Animal studies on sexual transmission of *T. gondii*.

First author, publication year, country	Species	Infection/mating setup	Sample size	Observed outcomes	Key findings
Dass et al[11], 2011, Singapore	Wistar rats (*Rattus norvegicus*)	① Epididymis cysts (n=5 males); cysts fed to females (4/4 seroconverted). ② Infected males mated with uninfected females (7 matings; 6/7 vaginal lavage positive; 4/4 females PCR+; 43/69 pups infected). ③ Behavioral preference: 12 pairs of males, 5-7 females each (72 trials); replicated in Long-Evans rats in SU, USA (n=36 females). ④ Competitive mating: 6 male pairs; reproductive performance evaluated in 11 infected *vs.* 11 control males.	Varied (see Infection/ Mating Setup)	Sexual and vertical transmission confirmed; vaginal shedding observed; infected males more attractive to females and gained more intromissions; infection did not impair fertility.	Infection both enhances male attractiveness and is sexually transmitted.
Arantes et al[13], 2009, Brazil	Dog	Ten mixed-breed males (18-19 months) experimentally inoculated with *T. gondii* (P and RH strains, *via* oocysts or tachyzoites). Semen analyzed by bioassay, PCR, and histology. 4 seronegative females were artificially inseminated with semen containing ~1×10^6 tachyzoites.	Males: ten; Females: four	Female one and two: early fetal reabsorption. Female 3: 2 pups (one stillborn, one survived 18 days). Female 4: 1 pup survived 7 days. All offspring tested positive for *T. gondii* cysts. Males: all seroconverted; parasite DNA and viable cysts detected in semen and testis/epididymis. Females: all seroconverted post-insemination.	Reports the first description of the isolation of *T. gondii* from the semen of experimentally infected dogs (confirmed by bioassay and PCR); infection caused sexual and vertical transmission, early pregnancy loss, and neonatal mortality.
Wanderley et al[14], 2015, Brazil	Saanen bucks (*Capra aegagrus hircus*)	1 buck orally infected with 2×10^5 oocysts of *T. gondii* (ME-49 strain); naturally mated with 5 multiparous crossbreds does. Control group: 1 uninfected buck mated with 5 does. Serology and PCR used to confirm infection in bucks, does, and offsprings.	Males: 2; Females: 10 (5 per group)	Infected group: 1 female experienced embryonic reabsorption, 1 female aborted at day 42, 3 females delivered full-term offsprings. PCR confirmed infection in 2/5 females and 4/5 offsprings. Control group: all females delivered healthy full-term offsprings. Infected buck showed transient clinical signs (apathy, hyporexia, coughing, fever, tachycardia).	Demonstrates semen-mediated and vertical transmission of *T. gondii* in goats; infection caused embryonic reabsorption, abortion, neonatal infection, and transient clinical illness in the buck.

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mia, whereas no such pattern was observed in non-smokers. Another study[26] reported that 40.3% of infertile men were IgG-positive for *T. gondii*, compared with only 16.1% of fertile men. The infected individuals showed lower sperm counts and more abnormal morphology, suggesting that infection may contribute to infertility.

However, not all evidence supports this association. A pilot study[27] of 60 men, including 15 seropositive individuals, found no significant differences in semen volume, sperm count, motility, or morphology between infected and uninfected groups. Nonetheless, indirect evidence continues to suggest

Table 1 (*continued*). Animal studies on sexual transmission of *T. gondii*.

First author, publication year, country	Species	Infection/mating setup	Sample size	Observed outcomes	Key findings
Liu et al[16], 2006, China	Rabbit	16 male rabbits infected with 1×10^5 RH tachyzoites *via* intraperitoneal injection; semen collected and mixed from 8 surviving males. 27 female rabbits divided into 4 groups with different vaginal health statuses, inseminated endovaginally with infected semen weekly for 8 weeks.	Males: 16 (8 died 8-14 days post-infection); Females: 27	ELISA detected anti-*T. gondii* antibodies in 7 females (25.9%). PCR detected B1 gene in 5 females (18.5%). Only 3 females were positive by both ELISA and PCR.	Confirms semen-mediated transmission of *T. gondii* in rabbits; vaginal health status did not affect transmission.
de Moraes et al[17], 2010, Brazil	Santa Inês sheep (*Ovis aries*)	Semen from seronegative male donor was experimentally contaminated with *T. gondii* tachyzoites (CPG strain, genotype III). Females inseminated *via* laparoscopy. Groups: G1: 6.5×10^4 tachyzoites, G2: 4×10^7 tachyzoites, G3: control (tachyzoite-free semen). Estrous synchronized with progestogen implants and eCG.	41 females divided into G1 (n=15), G2 (n=15) and G3 (n=11)	Seroconversion in G1: 5/15 (33.3%), G2: 15/15 (100%), G3: 0/11. *T. gondii* DNA detected in 93.3% (28/30) of infected groups. Hyperthermia in 100% of females in infected groups. Gestational outcomes: G1 – 9/15 embryonic reabsorption, 6/15 full-term delivery; G2 – 15/15 embryonic reabsorption; G3 – 8/11 full-term delivery.	Demonstrates *T. gondii* transmission *via* semen in sheep. Infection can lead to embryonic reabsorption and gestational loss, with severity depending on parasite dose.

a detrimental effect on fertility. For instance, one investigation[28] showed that 77 seropositive men fathered fewer children compared with 343 seronegative men.

Other studies have produced mixed results. In a cohort of eighty-three men, twenty-three tested positive for *T. gondii* antibodies, including twenty infertile patients. Six of these men were diagnosed with primary infertility and fourteen with secondary infertility. Despite these findings, no significant effect on reproductive parameters was observed[29]. Similarly, in a cohort of 260 men, infection rates were associated with epidemiological factors such as age, occupation, residence, animal contact, and number of children. The prevalence of infection was 45.16% in men with primary infertility, 53.33% in those with secondary infertility, and 47.37% among fertile controls. Conversely, non-infected individuals made up 54.83%, 46.66%, and 52.66% of these groups, respectively[30]. A larger study of four hundred apparently healthy men found seroprevalence rates of 30% for IgG and 2.5% for IgM. Infected men had significantly higher total and free testosterone levels, although no significant difference was observed in follicle-stimulating hormone levels (FSH)[31] (Table 2).

DIFFERENT MECHANISMS OF SPERM INJURY AFTER *T. GONDII* INFECTION

Sperm Decapitation

Following ingestion, *T. gondii* differentiates into tachyzoites, which replicate within parasitophorous vacuoles and spread throughout the host *via* the circulatory system. Since tachyzoites can invade nearly any nucleated cell type, the parasite is able to establish infection in multiple organs, including the gonads[32]. Testicular involvement is thought to occur through hematogenous spread, with parasites most likely breaching the BTB. The precise mechanisms and consequences of this barrier breach, however, remain unclear[9].

The BTB is formed by tight junctions between Sertoli cells at the base of the seminiferous tubules. It divides the tubules into two compartments. The basal compartment supports spermatogonial proliferation and differentiation, while the apical compartment, protected by the BTB, provides an immune-privileged space for meiosis, spermiogenesis, and spermiation[18]. Therefore, disruption of this barrier may expose developing germ cells to parasitic invasion, allowing *T. gondii* to interact directly with sperm (Figure 1).

Table 2 . Human studies on *T. gondii* and male fertility.

First author, publication year, country	Study design	Sample size	Observed outcomes	Key findings
Zhou et al[24], 2002, China	A case-control study to determine anti-*Toxoplasma* antibody levels and their association with infertility and antisperm antibody levels in infertile couples.	178 infertile couples, 190 fertile couples	Positive anti-*Toxoplasma* antibody: 34.83% infertile *vs.* 12.11% fertile; Positive anti-sperm antibody: 32.5% infected *vs.* 15.94% non-infected	*T. gondii* infection was associated with infertility and possibly mediated by anti-sperm antibodies contributing to pathogenesis.
Qi et al[25], 2005, China	A case-control study evaluating the association between *T. gondii* infection and male sterility.	One hundred infertile men, 100 fertile men	TOX-IgG: 7% infertile *vs.* 7% fertile; TOX-IgM: 16% infertile *vs.* 3% fertile; TOX-Cag (circulating antigen): 13% infertile *vs.* 1% fertile	*T. gondii* infection may affect male fertility and contribute to sterility; higher rates of IgM and CAg in infertile men suggest recent or active infection may be linked to impaired reproductive function.
Hlaváčová et al[2], 2021, Czech Republic	A cross-sectional study comparing the prevalence of *T. gondii* infection in men with and without semen pathology and examining its impact on semen parameters.	669 men (163 *Toxoplasma*-positive, 506 *Toxoplasma*-negative)	Higher incidence of fertility problems in infected men (48.47% *vs.* 42.29%); lower sperm concentration and motility in infected men; stronger effect in smokers.	Latent *T. gondii* infection was associated with reduced sperm count and motility, especially in smokers; no effect on sperm morphology or semen volume.
Eshraghi et al[26], 2023, Iran	A case-control study investigating the association between *T. gondii* infection and male infertility.	129 men (67 infertile, 62 fertile)	IgG seropositivity: 40.3% infertile *vs.* 16.1% fertile; IgM and PCR: no significant difference; association between infection and lower sperm count and abnormal morphology.	*T. gondii* infection may be a risk factor for male infertility; higher IgG prevalence in infertile men and its association with reduced sperm count and morphology suggest potential impact on reproductive parameters.
Colosi et al[27], 2015, Romania	A cross-sectional pilot study investigating the influence of *Toxoplasma gondii* infection on sperm and hormonal parameters in immuno-competent men.	60 men	TOX-IgG seropositivity: 25%; no significant differences in ejaculate volume, sperm count, motility, morphology, FSH, or testosterone between infected and uninfected men.	Latent *T. gondii* infection did not show significant impact on sperm or hormonal parameters in this pilot sample; limited sample size may have reduced statistical power.
Abdulla et al[29], 2015, Iraq	A cross-sectional study assessing the prevalence of chronic *T. gondii* infection in infertile and fertile men.	83 men (64 infertile: 25 primary, 39 secondary; 19 fertile controls)	IgG seropositivity: 27.7% overall; 20/64 infertile men positive (6 primary, 14 secondary); 3/19 controls positive; no significant differences in reproductive parameters.	*T. gondii* infection was not associated with changes in male reproductive parameters in this cohort, despite higher IgG prevalence in infertile men.
Al-Bajalan et al[30], 2015, Iraq	A cross-sectional study evaluating the prevalence of *T. gondii* infection and its association with infertility and epide-miological factors.	260 men	IgG/IgM seroprevalence: primary infertility 45.16%, secondary infertility 53.33%, fertile 47.37%; association found between infection and secondary infertility; infection also correlated with age, occupation, animal contact, residence, and number of children.	*T. gondii* infection was associated with secondary infertility and certain epidemiological factors; no clear impact on primary infertility or reproductive parameters reported.

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Recent research reveals that tachyzoites directly compromise sperm structure and function with profound implications for male fertility. In one *in vitro* study[9] using human sperm, exposure to tachyzoites at a multiplicity of infection of 0.5:1 led to a rapid increase in headless sperm. Within 5 minutes, headless sperm increased by 22%, and after 15 minutes, the proportion rose eightfold compared with controls. Electron microscopy confirmed major alterations, including plasma membrane disruptions, perforations in the sperm head, twisted tails and decapitated head-tail junctions. Furthermore, tachyzoites were

Table 2 (*continued*). Human studies on *T. gondii* and male fertility.

First author, publication year, country	Study design	Sample size	Observed outcomes	Key findings
Zghair et al[31], 2015, Iraq	A cross-sectional study assessing *T. gondii* seroprevalence and its effects on testosterone and FSH in healthy men.	400 apparently healthy blood donor males (10 IgM positive and 121 IgG positive as case group; 30 seronegative as control group)	IgG seroprevalence 30%, IgM 2.5%; total and free testosterone significantly higher in infected men; FSH showed no significant difference.	Both acute and chronic *T. gondii* infection were associated with higher total and free testosterone levels; no effect on FSH observed.

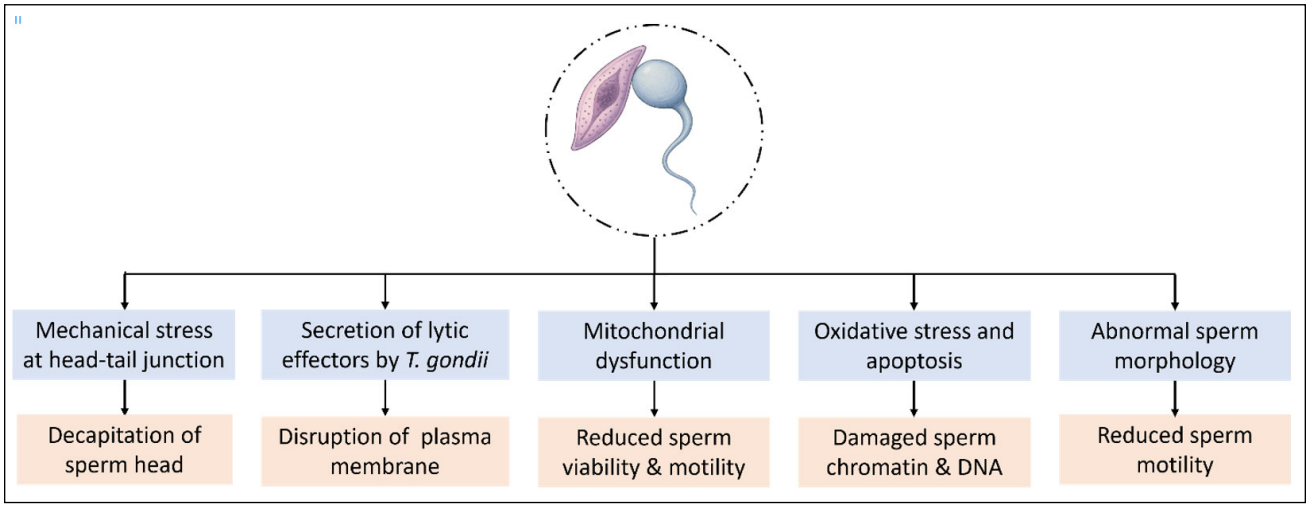

Figure 1. Mechanisms of *T. gondii*-induced injury to sperm.

observed attached to sperm heads *via* their apical invasion apparatus, implying an active assault rather than passive contact.

The tachyzoite stage is the most likely cause of this damage as it is motile, invasive, and secretes lytic effectors such as microneme and perforin-like proteins that disrupt host cell membranes[33]. Mechanical stress from parasite attachment and attempted invasion at the head-tail junction appears to be the immediate cause of sperm decapitation. While electron microscopy has not yet demonstrated intact internalization of tachyzoites into sperm heads, their attachment and membrane perturbation provide compelling evidence of direct interaction[9].

Animal studies support these findings. Tachyzoites have been detected in the testes and epididymis of rodents within 2-6 days of systemic infection following post-inoculation[34]. These parasites were confirmed to be viable and infective, indicating that sperm are indeed exposed to tachyzoites *in vivo*. The presence of tachyzoites in the male reproductive tract strongly suggests that *T. gondii* can directly target spermatozoa *in situ*.

Inflammatory and Oxidative Mechanisms

Infections of the male reproductive tract are well-recognized contributors to infertility. Inflammatory responses elevate pro-inflammatory cytokines that impair spermatogenesis, while inflammation-induced oxidative stress further compromises sperm function[35].

T. gondii infection triggers a Th1-dominant immune response, with activated macrophages producing reactive oxygen species (ROS) as part of the host defense. Although protective, excessive ROS production can damage sperm quality[36], and up to 80% of infertile men have been reported to show elevated ROS levels in semen samples[37].

Even in the absence of a measurable surge in ROS, tachyzoite interaction has been shown to reduce sperm viability, motility and mitochondrial membrane potential. This mitochondrial dysfunction undermines ATP production, which is essential for effective sperm motility and survival[9]. In parallel, animal studies showed that infected male mice and rats had significantly lower sperm motility, counts, and viability, as well as greater chromatin fragmentation and DNA damage[38].

These changes in semen parameters may represent collateral damage from parasite replication in immune-privileged reproductive tissues, or they may reflect parasite-driven manipulation aimed at improving transmission to the definitive host. One hypothesis is that reduced fertility may increase sexual activity, thereby enhancing the chances of sexual transmission[2]. It remains uncertain whether such effects occur solely in humans or also in natural intermediate hosts such as rodents.

Interestingly, *T. gondii* infection is associated with notable phenotypic changes in both humans and animals. Infected male rats display dominant behavior[39], while infected male students have been reported to be taller than uninfected controls[40]. Such traits could promote attractiveness and sexual opportunities, potentially enhancing sexual transmission across species.

Hormonal Alterations

Excessive ROS may also disrupt androgen regulation, lowering hormone levels required for spermatogenesis, testosterone synthesis, and overall sperm health[41]. In line with this, one case-control study[42] of 365 men with latent toxoplasmosis found significantly lower serum testosterone compared with uninfected controls. Experimental studies in mice have shown similar reductions in testosterone following infection[43].

Findings, however, remain inconsistent. Some studies have documented higher salivary testosterone in infected men[44] and indirect evidence of increased testosterone levels in young male cohorts[39,40]. Laboratory studies in rats have also reported elevated intratesticular testosterone 6-8 weeks after infection[45].

Higher testosterone levels following *T. gondii* infection could be partly associated with increased sexual behavior and sexual transmission of the parasite. On the other hand, declining testosterone levels following infection may be associated with impaired fertility, a pattern that has been observed in both infected humans and animals[46]. Collectively, the evidence suggests that *T. gondii* can influence reproductive function through its effects on testosterone. The direction of these changes, however, is inconsistent, and the mechanisms remain unclear.

DIAGNOSIS

Diagnosis of toxoplasmosis primarily relies on serologic testing, which remains the standard method in clinical settings. Detection of *T. gondii*-specific antibodies, particularly IgG and IgM, provides critical information regarding infection status[10]. A positive IgG result indicates previous or current exposure, while the presence of IgM suggests a recent infection. However, interpretation of IgM results can be challenging because these antibodies may persist for up to 18 months after the initial infection[1].

Polymerase chain reaction (PCR) is also widely used, especially for detecting parasite DNA in amniotic fluid or cerebrospinal fluid. This approach is valuable for diagnosing congenital infections *in utero* and central nervous system involvement in immunocompromised patients[10]. In rare cases, tachyzoites can be identified directly in clinical samples such as bronchoalveolar lavage fluid or lymph node biopsies. Although isolation of the parasite through intraperitoneal inoculation in mice or tissue culture is considered definitive, this method is rarely used because it is complex and impractical in clinical settings[1,10].

TREATMENT

Currently, there are no established treatment protocols specifically aimed at reversing reproductive complications of *T. gondii* infection in men. Standard antiparasitic regimens, including pyrimethamine, sulfadiazine and folinic acid and trimethoprim/sulfamethoxazole, are primarily reserved for severe systemic or ocular infections. Their effectiveness in addressing reproductive pathology remains unclear[10].

Several studies suggest that these drugs, particularly pyrimethamine, may negatively affect male reproductive function. Experimental studies in male mice and rats showed significant reductions in sperm motility and count following pyrimethamine treatment, along with structural changes in the testes and epididymis compared with control groups. Evidence also indicates that pyrimethamine may induce mutagenic effects in germ cells, impairing DNA synthesis in spermatogonia[47].

These findings are consistent with the known antifolate activity of pyrimethamine, which inhibits dihydrofolate reductase and disrupts nucleotide availability required for DNA replication. Similar fertility concerns have been raised for other anti-*Toxoplasma* drugs, including sulfadiazine and trimethoprim/sulfamethoxazole[47].

CONCLUSIONS

T. gondii is a widespread parasite with the potential to affect male reproductive health through multiple mechanisms, including direct interaction with sperm, disruption of the BTB, induction of oxidative stress, and hormonal alterations. While experimental and epidemiological studies provide evidence of impaired semen quality and possible sexual transmission, findings are often inconsistent and limited by small sample sizes or methodological differences.

Current treatments do not specifically target reproductive complications, and the safety of standard anti-*Toxoplasma* drugs with regard to male fertility remains uncertain. Overall, current data point to an intriguing but incompletely understood role of *T. gondii* in male infertility. Therefore, future research should focus on large-scale, well-controlled clinical studies to determine causality, improve diagnostic approaches and develop therapeutic interventions.

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Not applicable.

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