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CHRONIC TONSILLITIS AS A POTENTIAL SOURCE OF PROSTATIC INFLAMMATION AND MALE REPRODUCTIVE DYSFUNCTION: AN INTEGRATIVE PATHOPHYSIOLOGICAL HYPOTHESIS

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ABSTRACT

Background

Chronic tonsillitis is associated with persistent microbial and immunoinflammatory stimulation and may be linked to systemic inflammatory activity. Its possible role in

prostatic inflammation and male reproductive dysfunction remains insufficiently studied.

Aim

To formulate and pathophysiologically substantiate a hypothesis on the possible association between chronic tonsillitis, prostatic inflammation and male reproductive dysfunction.

Materials and Methods

A narrative conceptual review was conducted using publications identified in PubMed/MEDLINE, Scopus, Web of Science and Google Scholar up to March 31, 2026. The analysis included 89 sources published between 1993 and 2026.

Results

No direct clinical studies were identified that simultaneously evaluated chronic tonsillitis, prostatic inflammation and male reproductive function. The proposed model includes two possible pathways: a direct systemic effect of chronic tonsillar inflammation on the testis and spermatozoa and an indirect effect mediated by chronic prostatic inflammation. Individual components of the model are supported by data on systemic inflammation, oxidative stress, blood testis barrier disruption, altered spermatogenesis, immune dysregulation and chronic prostatic inflammation. The most hypothetical components remain tonsillar prostatic microbial translocation, migration of activated tonsillar lymphocytes, tonsillogenic induction of antisperm antibodies and specific epigenetic changes.

Conclusions

Chronic tonsillitis cannot be regarded as a proven cause of prostatic inflammation or male reproductive dysfunction. The presented model is a testable pathophysiological hypothesis and requires direct prospective clinical and experimental studies.

Keywords: chronic tonsillitis, chronic prostatitis, male reproductive dysfunction, systemic inflammation, oxidative stress, blood testis barrier, microbial translocation.

INTRODUCTION

Chronic tonsillitis is a persistent inflammatory disease of the palatine tonsils, in which long-term bacterial colonization of tonsillar crypts and biofilm formation may support local immune activation [1,11,17]. In addition to local inflammatory changes, chronic tonsillar disease may be associated with systemic inflammatory activity, and reductions in selected inflammatory markers have been reported after tonsillectomy or adenotonsillectomy [18,27,28].

The concept of chronically inflamed tonsils as a potential source of injury to distant organs is based on the theory of tonsillar focal infection and tonsil-induced immunoinflammatory disorders [2,14,15]. Similar mechanisms have been proposed in the pathogenesis of IgA nephropathy, psoriasis, rheumatoid arthritis, and other diseases [2,14,15]. However, the prostate gland and the male reproductive system remain insufficiently investigated as potential target organs of chronic tonsillar inflammation.

Chronic prostatitis and chronic pelvic pain syndrome are characterized by a complex and heterogeneous pathogenesis [3,51]. Infectious, immune, autoimmune, and neuroinflammatory mechanisms all contribute to the development of these conditions [3,4,51,52]. The persistence of clinical manifestations despite the absence of an infectious agent detectable by standard diagnostic methods in a proportion of patients supports the hypothesis that systemic inflammatory signals originating from distant chronic inflammatory foci may play a role. However, in the case of chronic tonsillitis, this potential association remains theoretical and has not yet been demonstrated.

The male reproductive system is highly susceptible to systemic inflammation and oxidative stress [12,29,30]. Male reproductive dysfunction may result both from the direct systemic effects of inflammation on the testes and spermatozoa [12,33–36] and from indirect mechanisms mediated by prostatic inflammation, alterations in the composition of seminal plasma, and changes in the local immune microenvironment [29,30,52]. However, direct clinical evidence demonstrating a causal relationship between chronic tonsillitis and these abnormalities is currently lacking.

Relevance

The rationale for the present study stems from the fact that, despite accumulating evidence of the systemic effects of chronic tonsillitis [18,27,28] and the established role of inflammation in the pathogenesis of prostatic and male reproductive disorders

[1,2,29,30,51,52], the potential relationship between chronic tonsillitis, prostatic inflammation, and male reproductive dysfunction has not yet been comprehensively evaluated from a pathophysiological perspective.

Novelty

The novelty of this study lies in the development of an integrative pathophysiological hypothesis linking chronic tonsillitis, prostatic inflammation, and male reproductive dysfunction. The proposed model incorporates both a direct systemic effect of chronic tonsillar inflammation on the male reproductive system and a potential indirect effect mediated through prostatic inflammation. Rather than asserting a proven causal relationship, the model provides a testable conceptual framework for future experimental and clinical investigations.

AIM

To formulate and provide a pathophysiological rationale for the hypothesis of a possible association between chronic tonsillitis, prostatic inflammation, and male reproductive dysfunction.

Research Objectives

1. To characterize chronic tonsillitis as a potential source of systemic inflammatory burden.
2. To analyze the potential association between chronic tonsillitis and prostatic inflammation.
3. To evaluate the potential mechanisms by which systemic and prostatic inflammation may contribute to male reproductive dysfunction.
4. To integrate the available evidence into a pathophysiological model and identify the limitations of this model.

MATERIALS AND METHODS

This study was conducted as a narrative conceptual review. The objective of the review was to formulate and provide a pathophysiological rationale for the hypothesis of

a possible association between chronic tonsillitis, prostatic inflammation, and male reproductive dysfunction.

A literature search was performed in PubMed/MEDLINE, Scopus, and Web of Science without restriction on the starting date through March 31, 2026. Google Scholar was additionally used to identify relevant publications and to screen the reference lists of included studies. The included literature was published between 1993 and 2026.

The main search terms included chronic tonsillitis, tonsillar focal infection, tonsillar microbiota, tonsillar biofilm, systemic inflammation, oxidative stress, microbial translocation, bacteremia, endotoxemia, chronic prostatitis, chronic pelvic pain syndrome, prostatic inflammation, male infertility, semen quality, blood–testis barrier, Sertoli cells, Leydig cells, steroidogenesis, spermatogenesis, molecular mimicry, antisperm antibodies, and seminal microbiome. Search terms were combined using the Boolean operators AND and OR according to the specific component of the proposed hypothesis being investigated.

The review included original clinical and experimental studies, systematic reviews, meta-analyses, narrative reviews, and selected foundational publications that provided evidence relevant to one or more components of the proposed hypothesis, including chronic tonsillitis, systemic inflammation, microbial translocation, chronic prostatic inflammation, male reproductive dysfunction, the blood–testis barrier, steroidogenesis, spermatogenesis, semen parameters, and autoimmune mechanisms. Studies involving humans, animal models, and cell culture models were considered. The inclusion of experimental studies was justified by the limited availability of direct clinical evidence addressing the proposed association.

Duplicate records, publications not aligned with the objective of the review, and studies lacking data on the inflammatory, immunological, microbial, oxidative, neuroendocrine, or reproductive mechanisms under consideration were excluded. After removal of duplicate and irrelevant records, a total of 89 publications were included in the final analysis.

Data were synthesized using a thematic approach. The evidence was conceptually classified into three levels: (1) evidence directly related to chronic tonsillitis; (2) evidence describing corresponding mechanisms involved in prostatic inflammation or male reproductive dysfunction; and (3) hypothetical links derived through pathophysiological extrapolation.

In the final stage, the available evidence was integrated into a pathophysiological model comprising two potential pathways: (1) a direct systemic effect of chronic tonsillar inflammation on male reproductive function and (2) an indirect effect mediated through prostatic inflammation.

A formal assessment of the risk of bias and a standardized quality appraisal of the included publications were not performed. Likewise, no statistical pooling of results or meta-analysis was conducted because this study was designed as a narrative conceptual review integrating methodologically heterogeneous clinical, experimental, and review studies.

RESULTS

A total of 89 unique publications published between 1993 and 2026 were included in the final analysis. The reviewed literature comprised clinical and epidemiological studies, experimental studies using animal and cell culture models, systematic and narrative reviews, meta-analyses, and selected foundational investigations. No clinical studies were identified that specifically evaluated the association between chronic tonsillitis, prostatic inflammation, and male reproductive dysfunction simultaneously. Therefore, the findings were synthesized according to the individual pathophysiological mechanisms underlying the proposed association.

Chronic Tonsillitis as a Source of Persistent Microbial and Immunoinflammatory Stimulation

Studies of tonsillar tissue have shown that, in chronic and recurrent inflammation, the crypts of the palatine tonsils harbor polymicrobial communities and bacterial biofilms. These biofilms contain Fusobacterium nucleatum, Streptococcus spp., Prevotella spp., Porphyromonas spp., and other microorganisms capable of sustaining prolonged activation of both the innate and adaptive immune systems [4,11,37].

Functional alterations of T lymphocytes and impaired local immune regulation have been described in chronically inflamed tonsillar tissue [17,54]. In several diseases, chronically inflamed tonsils are regarded as a potential source of systemic autoimmune or inflammatory responses, accompanied by immune cell activation and pathological processes affecting distant organs [3,14,15].

Indirect evidence of the systemic effects of chronic tonsillar inflammation includes alterations in the neutrophil-to-lymphocyte ratio (NLR), lymphocyte-to-monocyte ratio (LMR), and platelet-to-lymphocyte ratio (PLR), as well as reductions in selected inflammatory markers following tonsillectomy or adenotonsillectomy [18,27,28]. In one study, the neutrophil-to-lymphocyte ratio decreased significantly after tonsillectomy ($p = 0.045$), and postoperative values did not differ significantly from those of the control group ($p = 0.584$) [27]. In a meta-analysis, adenotonsillectomy was associated with a reduction in C-reactive protein levels, with a standardized mean difference of −0.946 (95% CI, −1.578 to −0.314) [28]. These findings support the presence of a systemic inflammatory burden associated with chronic tonsillar inflammation but do not demonstrate a direct effect on the prostate gland or the male reproductive system.

Potential Dissemination of Microorganisms and Bacterial Components

The available literature supports the biological plausibility of hematogenous and lymphatic dissemination of microorganisms from oropharyngeal infectious foci [5,6]. For Streptococcus pyogenes, experimental studies have demonstrated extracellular dissemination through lymphatic vessels and lymph nodes, followed by entry into the systemic circulation [6]. In chronic inflammatory diseases of the oral cavity, translocation of bacterial components into the bloodstream, including lipopolysaccharide (LPS), has also been described [7,8].

However, no direct evidence was identified demonstrating the translocation of bacteria from the tonsillar crypts to the prostate gland or seminal fluid. Therefore, tonsil-to-prostate microbial translocation remains a hypothetical component of the proposed pathophysiological model.

Immunoinflammatory Mechanisms of Chronic Prostatic Inflammation

Studies of chronic prostatitis and chronic pelvic pain syndrome have consistently demonstrated evidence of cytokine activation, immune dysregulation, and autoimmune responses [1,2,51,52]. A meta-analysis including 34 studies reported increased levels of TNF-α, IL-1β, IL-6, and IL-8 in the majority of biological samples obtained from patients with chronic prostatitis/chronic pelvic pain syndrome, as well as in experimental models [51].

In experimental autoimmune prostatitis, IL-6 was shown to impair the function of regulatory T cells and exacerbate the Th17/Treg imbalance [1]. In patients with chronic pro-

statitis/chronic pelvic pain syndrome, Th1- and Th17-mediated immune responses directed against prostatic and seminal antigens have also been identified [52].

Activation of NF-κB and STAT3 signaling pathways, involvement of TLR4-mediated signaling, reactive oxygen species (ROS)-dependent alterations, and the establishment of self-sustaining inflammatory cascades have been described in prostatic tissue and experimental models [22,23,25]. These findings support the existence of persistent inflammatory mechanisms underlying chronic prostatic inflammation but do not indicate that the initiating inflammatory signals originate from chronic tonsillar disease.

Thus, prostatic inflammation may persist even in the absence of an infectious agent detectable by standard diagnostic methods. This provides a pathophysiological basis for the hypothesis that systemic inflammatory signals originating from a distant chronic inflammatory focus may amplify or sustain local inflammation within the prostate gland.

Bacterial DNA and the Prostatic Microbiota

In a study of prostate tissue, bacterial DNA sequences were detected in 79 of 170 patients with chronic prostatitis (46.4%) and in 21 of 107 patients with prostate cancer (19.6%) ($p < 0.0001$) [21]. These findings demonstrate the presence of bacterial genetic material in prostatic tissue in a substantial proportion of patients with chronic inflammation.

However, the detection of bacterial DNA does not establish the presence of viable microorganisms, active infection, or a tonsillar origin of the detected bacteria. Therefore, these findings should be regarded only as indirect evidence supporting a possible contribution of microbial factors to prostatic inflammation.

Association between Chronic Prostatic Inflammation and Male Reproductive Function

In patients with chronic prostatitis/chronic pelvic pain syndrome, autoreactive Th1- and Th17-mediated immune responses directed against prostatic and seminal antigens have been associated with impaired semen quality [52]. Prostatic inflammation may adversely affect male reproductive function through multiple mechanisms, including alterations in the composition of seminal plasma, increased local oxidative stress, cytokine- and immune cell-mediated damage to spermatozoa, and impaired secretory function of the prostate gland [29,30,36,52].

Studies of the seminal microbiome and genital tract infections have also shown that the presence of pathogenic microorganisms and chronic infectious burden may be associated with alterations in sperm concentration, motility, and other semen parameters [41,82,85]. However, these findings do not establish a specific role for chronic tonsillitis.

The key studies forming the evidence base for the proposed pathophysiological model are summarized in Table 1.

Table 1. Key evidence supporting the hypothesis

EVIDENCE BLOCK	MAIN FINDING	RELEVANCE TO THE HYPOTHESIS	SOURCES
Tonsillar microbiota and biofilms	Polymicrobial communities and biofilms are present in tonsillar tissue.	Supports chronic microbial stimulation in the tonsils.	[4, 11]
Tonsillar immune changes	Altered T cell function and immune cell distribution were described in chronic tonsillar disease.	Supports local immune dysregulation in chronic tonsillitis.	[17, 54]
Systemic inflammation after tonsil disease	Inflammatory blood markers decreased after tonsillectomy or adenotonsillectomy.	Supports a possible systemic inflammatory component.	[18, 27, 28]
Oral inflammation and prostate disease	Periodontal disease was associated with prostatitis, and oral microbial DNA was found in prostatic secretion in some patients.	Provides indirect support for an oral prostatic inflammatory link.	[9, 19]
Bacterial DNA in prostate tissue	Bacterial DNA was detected in prostate tissue in chronic prostatitis.	Supports microbial involvement in prostatic inflammation, but not tonsillar origin.	[21]
Cytokines in chronic prostatitis	TNF alpha, IL 1 beta, IL 6 and IL 8 were increased in most studied samples.	Supports inflammatory activation in chronic prostatitis.	[51]
Immune dysregulation in prostate inflammation	IL 6, Th17 and Treg imbalance, NF kB, STAT3, TLR4 and ROS related pathways were implicated.	Supports immune and molecular mechanisms of chronic prostatic inflammation.	[1, 22, 23, 25]
Prostatic inflammation and semen quality	Autoreactive Th1 and Th17 responses were associated with poorer semen quality.	Links prostatic immune inflammation with male reproductive dysfunction.	[52]
Testicular barrier and spermatogenesis	IL 6 and LPS impaired blood testis barrier integrity, steroidogenesis and spermatogenesis in experimental models.	Supports a possible pathway from inflammation to impaired male fertility.	[33, 34, 35]
Oral inflammation and semen abnormalities	Moderate or severe periodontitis was associated with higher odds of semen abnormalities.	Provides indirect clinical support for a link between oral inflammation and semen quality.	[78]
Endotoxin and testosterone	Low dose endotoxin induced inflammation and later reduced testosterone.	Supports possible suppression of Leydig cell function during systemic inflammation.	[86]
Mast cells in chronic pelvic pain	Mast cell targeted treatment reduced active tryptase and symptom score.	Supports mast cell involvement in chronic pelvic pain, without proving tonsillar origin.	[59]

The available evidence supports the individual components of chronic tonsillar, prostatic, and reproductive inflammation. However, no studies have directly evaluated the entire proposed sequence linking chronic tonsillitis to prostatic inflammation and, subsequently, to male reproductive dysfunction.

Systemic Inflammation, Oxidative Stress, and Sperm Damage

Oxidative stress is one of the best-established mechanisms underlying male infertility [12,13,16,29,30]. Excessive production of reactive oxygen species (ROS) can damage sperm membrane lipids, proteins, and DNA, impair the acrosome reaction, and reduce the functional competence of spermatozoa [12,13,16]. The high susceptibility of spermatozoa to oxidative injury is largely attributable to their high content of polyunsaturated fatty acids and their limited intracellular antioxidant defenses [12,13,16].

Chronic inflammation and infectious processes can exacerbate oxidative stress and the associated damage to male germ cells [29,30,36]. However, no studies were identified demonstrating increased oxidative sperm damage specifically in men with chronic tonsillitis. Therefore, the proposed sequence linking chronic tonsillar inflammation to systemic oxidative stress and subsequent sperm damage is biologically plausible but is currently supported only by indirect evidence.

Disruption of the Blood–Testis Barrier and Testicular Cell Function

Experimental studies have demonstrated that IL-6 can impair the integrity of the blood–testis barrier and alter the localization of tight junction proteins in Sertoli cells [33,34]. In a model of autoimmune orchitis, IL-6 exposure was associated with seminiferous tubule damage and increased permeability of the blood–testis barrier [34].

TNF-α and bacterial lipopolysaccharide (LPS) have also been shown to exert damaging effects on the testis and epididymis [35,36]. In an experimental model, LPS-induced inflammation disrupted spermatogenesis, steroidogenesis, and blood–testis barrier permeability, whereas the absence of TNF-α or its pharmacological inhibition reduced the severity of these alterations [35].

These findings demonstrate that inflammatory mediators and bacterial components can damage testicular structures in experimental models. However, it remains unclear whether such mediators and components reach concentrations during chronic tonsillitis that are sufficient to disrupt the blood–testis barrier or impair testicular cell function.

Endocrine Mechanisms

Clinical and experimental studies have demonstrated that endotoxin-induced inflammation may reduce testosterone production [86]. In healthy men, administration of low-dose endotoxin was associated with an inflammatory response and subsequent decline in testosterone levels without corresponding changes in luteinizing hormone or follicle-stimulating hormone concentrations, suggesting a potential direct inhibitory effect on Leydig cell function [86].

Proinflammatory cytokines may also disrupt the regulation of the hypothalamic–pituitary–gonadal axis and testicular steroidogenesis [86–88]. However, no direct evidence of altered reproductive hormone profiles in men with chronic tonsillitis was identified in the reviewed literature. Therefore, the endocrine pathway represents a plausible but currently unproven component of the proposed hypothesis.

Autoimmune Mechanisms and Antisperm Antibodies

Disruption of the blood–testis barrier may lead to the exposure of germ cell antigens and the development of autoimmune responses [31,32]. Antisperm antibodies can bind to surface antigens of spermatozoa and impair their motility, including through mechanisms involving sperm agglutination and immobilization [39,40].

The literature describes cross-reactivity between carbohydrate antigenic determinants of spermatozoa, somatic cells, and infectious agents [39]. Streptococcal infections may also be associated with autoimmune reactions mediated by molecular mimicry mechanisms [76]. However, specific cross-reactivity between antigens of tonsillar microorganisms and antigens of spermatozoa or testicular tissues has not been directly investigated.

Thus, tonsil-derived induction of antisperm antibodies remains a hypothetical mechanism. Available evidence supports the possibility of autoimmune responses following disruption of the immunological isolation of the testis and demonstrates the presence of shared antigenic determinants between spermatozoa and infectious agents; however, it does not prove that chronic tonsillitis leads to the formation of antisperm antibodies [31,32,39].

Epigenetic Alterations

Epigenetic mechanisms play an important role in the regulation of spermatogenesis and male reproductive function [63–66]. Oxidative stress may also contribute to epigenetic alterations affecting sperm function [67].

In chronic prostatitis/chronic pelvic pain syndrome, epigenetic changes have been described in immunoregulatory loci, including IL10, FOXP3, CD274, and TNF [55], as well as hypermethylation of promoter regions of ESR1 and ESR2 in somatic cells of ejaculate [56].

No data were identified regarding specific epigenetic alterations in spermatozoa, testicular cells, or immune cells in men with chronic tonsillitis. Therefore, the epigenetic component should be regarded only as an additional hypothetical mechanism rather than an established consequence of chronic tonsillar inflammation.

Evidence from Tonsillectomy Studies

Following tonsillectomy and adenotonsillectomy, reductions in systemic inflammatory markers have been reported in several studies. In patients with chronic tonsillitis, the neutrophil-to-lymphocyte ratio decreased significantly after tonsillectomy ($p = 0.045$) [27]. Another study demonstrated reductions in both neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios after adenotonsillectomy [18]. A meta-analysis showed that adenotonsillectomy in children with obstructive sleep apnea was associated with decreased C-reactive protein levels [28]. However, these studies differed in terms of surgical indications and patient characteristics.

In a large national cohort study including 179,875 patients who underwent tonsillectomy, the standardized incidence ratio for autoimmune diseases was 1.34 (95% CI, 1.30–1.37) [68]. In another population-based cohort study, surgical removal of lymphoid tissue of the Waldeyer ring was associated with an increased risk of Sjögren syndrome (HR 1.52; 95% CI, 1.23–1.87). Among individuals who underwent surgery before the age of 18 years, the hazard ratio was 2.27 [69].

These findings do not support considering tonsillectomy as a therapeutic strategy for correcting prostatic inflammation or male reproductive dysfunction in the absence of dedicated clinical studies. They demonstrate reductions in selected inflammatory markers after surgery but also highlight the complexity and potential ambiguity of its long-term immunological consequences.

Integrative Pathophysiological Model

Synthesis of the available evidence allowed the identification of two major pathways through which chronic tonsillitis may potentially influence male reproductive function.

The first pathway involves a direct systemic effect of the chronic tonsillar inflammatory focus. Persistent polymicrobial communities and biofilms within tonsillar crypts may sustain local microbial and immune stimulation [4,11,17,37]. The reduction of selected inflammatory markers following tonsillectomy indirectly suggests a possible systemic component of this inflammatory process [18,27,28]. Potential consequences of such systemic inflammatory burden may include oxidative damage to spermatozoa, disruption of the blood–testis barrier, alterations in Sertoli and Leydig cell function, impaired steroidogenesis and spermatogenesis, as well as autoimmune responses resulting from disruption of the immunological isolation of the testis [12,13,16,29,30,31,32,33–36,39,40,86–88].

The second pathway involves an intermediate role of the prostate gland. The potential contribution of oral inflammatory foci to prostatic inflammation is indirectly supported by studies of periodontitis and by the detection of bacterial DNA in prostate tissue [9,10,19,21]. Systemic inflammatory signals may amplify or sustain prostatic inflammatory and immune pathways [1,22,23,25,51]. Chronic prostatic inflammation, in turn, may be associated with autoreactive Th1- and Th17-mediated responses against prostatic and seminal antigens, as well as impaired semen quality [52].

The most strongly supported components of the proposed model include the presence of polymicrobial communities and immune alterations in tonsillar tissue [4,11,17,37], reductions in selected inflammatory markers following tonsillectomy [18,27,28], the role of inflammatory mediators and signaling pathways in prostatic and testicular inflammation [1,22,23,25,33–36,51], the detrimental effects of oxidative stress on spermatozoa [12,13,16,29,30], and the association between chronic prostatitis/chronic pelvic pain syndrome and impaired semen quality [52].

The most hypothetical components remain direct tonsil-to-prostate microbial translocation, migration of activated tonsillar lymphocytes to the prostate gland, tonsil-derived induction of antisperm antibodies, and specific epigenetic alterations affecting the reproductive system.

The key pathophysiological components of the proposed model are presented in Table 2, while the levels of supporting evidence are summarized in Table 3. The present analysis indicates that the model is based on established individual pathophysiologi-

cal mechanisms and indirect evidence; however, the overall association between chronic tonsillitis, prostatic inflammation, and male reproductive dysfunction remains hypothetical and requires direct experimental and clinical validation.

Table 2. Main pathophysiological links in the proposed model

PATHOPHYSIOLOGICAL LINK	MAIN MECHANISM	POSSIBLE CONSEQUENCE	EVIDENCE STATUS	SOURCES
Chronic microbial and immune stimulation in tonsils	Polymicrobial communities, biofilms and local immune activation in tonsillar tissue	Persistent local inflammation and possible systemic inflammatory load	Supported in chronic tonsillar disease	[4,11,17,37,54]
Systemic inflammation	Changes in inflammatory blood indices and reduction of some inflammatory markers after tonsillectomy or adenotonsillectomy	Possible inflammatory effects on distant organs	Supported for systemic inflammatory activity; reproductive effects not shown	[18,27,28]
Microbial or bacterial component translocation	Possible spread of microorganisms or bacterial components from oral inflammatory sites	Possible immune activation in the prostate	Indirect evidence; tonsil to prostate translocation remains hypothetical	[5–10,19,21]
Prostatic cytokine activation	Increased IL 6, TNF α, IL 1β and IL 8	Maintenance of chronic prostatic inflammation	Supported in chronic prostatitis/chronic pelvic pain syndrome	[1,2,51,52]
NF κB, STAT3, TLR4 and ROS related pathways	Activation of inflammatory signalling and self maintaining inflammatory cascades	Persistence of prostatic inflammation	Supported mainly in experimental models	[22,23,25]
Th17/Treg imbalance and autoreactive responses	IL 6 related Treg dysfunction and Th1/Th17 responses to prostate and semen antigens	Autoimmune inflammation and poorer semen quality	Supported in prostatic inflammation; tonsillar origin not shown	[1,2,51,52]
Oxidative stress	Excess reactive oxygen species and damage to sperm lipids, proteins and DNA	Reduced sperm motility, viability and fertilizing capacity	Supported in male reproductive dysfunction; link with chronic tonsillitis is indirect	[12,13,16,29,30,36]
Blood testis barrier injury	Effects of IL 6, TNF α and lipopolysaccharide on Sertoli cell junctions	Impaired spermatogenic microenvironment and exposure of germ cell antigens	Supported in experimental models; chronic tonsillitis data absent	[33–35]
Sertoli and Leydig cell dysfunction	Inflammatory and endotoxin mediated injury of Sertoli and Leydig cells	Impaired spermatogenesis, steroidogenesis and testosterone production	Supported in inflammatory models; tonsillar origin not proven	[33–36,86–88]
Autoimmune mechanisms and antisperm antibodies	Loss of immune isolation and possible cross reactive antigenic mechanisms	Possible antisperm antibody formation and impaired sperm motility	General mechanisms supported; tonsillogenic induction remains hypothetical	[31,32,39,40,76]
Epigenetic mechanisms	Epigenetic regulation of spermatogenesis and inflammation related epigenetic changes	Possible persistence of inflammatory or reproductive phenotype	Additional hypothetical mechanism; chronic tonsillitis data absent	[55,56,63–67]

Table 3. Levels of evidence supporting the proposed pathophysiological model

EVIDENCE LEVEL	CATEGORY	CONTENT
Direct evidence for separate links	Confirmed or proposed links	Tonsillar microbial and immune stimulation; systemic inflammatory activity in chronic tonsillitis; inflammatory mechanisms in chronic prostatitis; impaired semen quality; inflammatory injury of the blood testis barrier, spermatogenesis and steroidogenesis
Direct evidence for separate links	Main data	Tonsillar biofilms, T cell changes, inflammatory blood indices, cytokine activation, Th17/Treg imbalance, NF kB and STAT3 activation, autoreactive Th1 and Th17 responses, and experimental injury of the blood testis barrier and testicular function
Direct evidence for separate links	Meaning for the model	Supports the biological plausibility of separate parts of the model
Direct evidence for separate links	Main limitation	The complete pathway from chronic tonsillitis to prostatic inflammation and male reproductive dysfunction has not been directly studied
Direct evidence for separate links	Sources	[1,4,11,17,18,22,23,25,27,28,33–35,51,52,54,86]
Indirect evidence	Confirmed or proposed links	Possible spread of microorganisms or bacterial components from chronic oropharyngeal inflammation; links between oral inflammation, prostate disease, semen abnormalities and systemic endocrine effects
Indirect evidence	Main data	Periodontitis was associated with prostatitis and semen abnormalities; oral microbial DNA was detected in prostatic secretion in some patients; bacterial DNA was found in prostate tissue; endotoxin was associated with inflammation and reduced testosterone
Indirect evidence	Meaning for the model	Supports the plausibility of oral prostatic and systemic reproductive pathways
Indirect evidence	Main limitation	These data were obtained mainly from periodontitis, endotoxemia, urogenital infections and other inflammatory conditions, not from chronic tonsillitis
Indirect evidence	Sources	[5–10,12,13,16,19,21,29,30,36,62,77,78,85–89]
Hypothetical links	Confirmed or proposed links	Tonsil to prostate microbial transfer; systemic amplification of prostatic inflammation by a tonsillar focus; migration of activated tonsillar lymphocytes; tonsillogenic induction of antisperm antibodies; molecular mimicry; reproductive epigenetic changes
Hypothetical links	Main data	These links are inferred from data on focal infection, autoimmune inflammation, blood testis barrier injury, cross reactive antigens and epigenetic changes in chronic prostatitis and male infertility
Hypothetical links	Meaning for the model	Defines the testable part of the hypothesis

Hypothetical links	Main limitation	Direct clinical or experimental evidence for these mechanisms in chronic tonsillitis is absent
Hypothetical links	Sources	[3,14,15,31,32,39,40,55,56,63–67,76]

DISCUSSION

This narrative conceptual review integrates evidence on chronic tonsillitis, prostatic inflammation, and male reproductive dysfunction into a pathophysiological model. The analysis does not establish a direct causal relationship between these conditions but demonstrates the biological plausibility of such an association based on the individual mechanisms discussed in the preceding sections.

A key feature of the proposed model is the distinction between two potential pathways through which chronic tonsillitis may influence male reproductive function. The first pathway involves a direct systemic effect of inflammatory, bacterial, and oxidative factors on the testes and spermatozoa [12,33–36]. The second pathway involves an indirect role of the prostate gland, in which systemic inflammatory signals or potential microbial translocation may contribute to the persistence of chronic inflammation and affect semen quality [21,51,52].

Within the direct pathway, the role of systemic inflammation and oxidative stress is the most strongly supported component. These mechanisms have been extensively investigated in inflammatory diseases, urogenital infections, and other conditions associated with male infertility [12,29,30,36]. However, direct evidence demonstrating comparable sperm damage specifically in the context of chronic tonsillitis is currently lacking.

A potentially important component of the proposed model is disruption of the blood–testis barrier. Experimental data indicate that IL-6, TNF-α, and lipopolysaccharide can increase the permeability of this barrier and impair the microenvironment required for normal spermatogenesis [33–35]. Such disruption may also promote the exposure of germ cell antigens to the immune system, thereby creating conditions conducive to autoimmune responses and the formation of antisperm antibodies [31,32,39].

The endocrine component of the proposed model is also biologically plausible. Endotoxin-induced inflammation and proinflammatory cytokines may impair testosterone production, Leydig cell function, and regulation of the hypothalamic–pituitary–gonadal axis [86–88]. However, studies simultaneously assessing reproductive hor-

mone profiles and spermatogenic parameters in men with chronic tonsillitis are currently lacking. Therefore, the endocrine pathway remains an extrapolation of findings obtained in other inflammatory conditions.

The indirect pathway involving the prostate gland has independent pathophysiological relevance. Chronic prostatitis and chronic pelvic pain syndrome are characterized by cytokine activation, immune dysregulation, and self-sustaining inflammatory cascades [1,2,51,52]. These processes may persist even in the absence of detectable bacterial infection. Therefore, systemic inflammatory signals originating from a distant chronic inflammatory focus could theoretically amplify pre-existing prostatic inflammation or lower the threshold for its transition to a chronic state.

The association between chronic prostatic inflammation and impaired semen quality is of particular importance for the proposed model. In patients with chronic prostatitis/chronic pelvic pain syndrome, autoreactive Th1- and Th17-mediated responses against prostatic and seminal antigens have been associated with reduced semen quality [52]. Therefore, the prostate gland may represent a potential intermediate link between systemic inflammatory exposure and impaired male reproductive function.

The hypothesis of microbial translocation requires cautious interpretation. The possibility of hematogenous and lymphatic dissemination of microorganisms from oropharyngeal foci has been demonstrated [5,6], and bacterial DNA has been detected in prostate tissue in a proportion of patients with chronic prostatitis [21]. However, direct evidence of microbial translocation from tonsillar crypts to prostatic tissue or seminal fluid is currently lacking. Therefore, tonsil-to-prostate microbial translocation remains a hypothetical mechanism and requires molecular confirmation through identification of identical microbial strains.

The autoimmune component of the proposed model also remains largely hypothetical. Streptococcal infections may trigger autoimmune responses through molecular mimicry mechanisms [76], chronically inflamed tonsils are considered a potential source of systemic immune activation in certain diseases [3,14,15], and cross-reactivity has been described between some bacterial and sperm-associated carbohydrate epitopes [39]. However, specific cross-reactivity between antigens of tonsillar microorganisms and components of the male reproductive system has not been directly investigated.

Epigenetic mechanisms may contribute to the long-term persistence of inflammatory or reproductive phenotypes. In chronic prostatitis/chronic pelvic pain syndrome, epi-

genetic alterations in immunoregulatory loci and estrogen receptor genes have been described in somatic cells of ejaculate [55,56]. Alterations in epigenetic regulation have also been reported in male infertility, while oxidative stress is considered a potential contributor to epigenetic dysregulation in spermatozoa [63–67]. However, evidence of specific epigenetic effects induced by chronic tonsillitis is currently lacking. Therefore, this component should be regarded as a potential area for future research rather than an established mechanism.

Validation of the proposed model requires a series of well-designed clinical and experimental studies. At the initial stage, men with chronic tonsillitis should be compared with control groups regarding semen parameters, sperm DNA fragmentation, antisperm antibodies, oxidative stress markers, reproductive hormone profiles, and systemic cytokine patterns. Chronic prostatitis or chronic pelvic pain syndrome should be evaluated separately as a potential intermediate factor.

Further studies should include assessment of changes in these parameters following treatment of chronic tonsillitis, parallel sequencing of the microbiota of tonsillar crypts, prostatic secretions, and seminal fluid, as well as investigation of cross-reactivity between tonsillar bacterial antigens and sperm antigens.

Thus, the proposed model demonstrates internal pathophysiological coherence and integrates several established mechanisms of systemic, prostatic, and reproductive inflammation. However, a causal relationship has not yet been demonstrated. Chronic tonsillitis should not be considered an established cause of male reproductive dysfunction but rather a potential source of systemic inflammatory burden, the clinical significance of which requires dedicated investigation.

Practical Implications

The practical significance of the proposed model lies in the development of new directions for clinical assessment and scientific investigation rather than in modifying current therapeutic approaches. In men with chronic tonsillitis accompanied by reproductive dysfunction or chronic pelvic pain, evaluation of systemic inflammatory markers, prostate status, and semen parameters may be considered as part of standard diagnostic assessment. However, the available evidence does not support recommending tonsillectomy or other treatments for chronic tonsillitis as a primary strategy for correcting prostatic inflammation or male reproductive dysfunction. Clinical decisions should remain based on established indications, while the proposed model may serve

as a framework for patient selection and outcome assessment in future prospective studies.

Limitations

This study has several limitations.

First, the review was conducted as a narrative conceptual analysis. A formal assessment of the risk of bias and a standardized quality appraisal of the included studies were not performed, limiting the ability to quantitatively compare findings and determine the overall strength of the available evidence.

Second, the reviewed literature lacked direct clinical studies simultaneously evaluating chronic tonsillitis, prostatic inflammation, and male reproductive function. A substantial proportion of the proposed model is based on the integration of evidence obtained separately from studies of chronic tonsillitis, chronic prostatitis, systemic inflammation, experimental orchitis, periodontitis, and male infertility.

Third, part of the available evidence has been derived from animal models and cell culture studies. The concentrations of cytokines, lipopolysaccharide, and other inflammatory mediators used in these experimental systems may not correspond to the levels present in chronic tonsillitis in humans. Therefore, translation of these findings into clinical settings requires cautious interpretation.

Fourth, the detection of bacterial DNA in prostate tissue or prostatic secretions does not demonstrate the presence of viable microorganisms, active infection, or their origin from a tonsillar focus [9,21]. The reviewed studies did not include molecular comparison of microorganisms from tonsillar crypts and the prostate at the level of identical microbial strains.

Fifth, autoimmune and epigenetic mechanisms have not been directly investigated in the context of chronic tonsillitis. There are no data demonstrating specific cross-reactivity between tonsillar bacterial antigens and sperm or testicular tissue antigens, nor are there established epigenetic signatures characteristic of men with chronic tonsillitis.

Sixth, the included studies were heterogeneous in terms of study design, populations, diagnostic criteria, and methods used to assess inflammation, microbiota, and semen parameters. This heterogeneity limits direct comparison of findings and precludes justified statistical pooling of the available data.

Seventh, the influence of potential confounding factors cannot be excluded, including age, obesity, smoking, varicocele, metabolic disorders, urogenital infections, medication use, and other chronic inflammatory conditions.

Therefore, the proposed pathophysiological model should be regarded as a testable hypothesis rather than an established causal relationship.

CONCLUSIONS

1. Chronic tonsillitis may be considered a potential source of persistent microbial and immunoinflammatory stimulation, which may be associated with systemic inflammatory activity and the release of bacterial components into the bloodstream.
2. Prostatic inflammation may theoretically be sustained by systemic inflammatory signals originating from a distant chronic inflammatory focus through cytokine activation, immune dysregulation, and self-perpetuating inflammatory cascades. Direct tonsil-to-prostate microbial translocation, however, has not been demonstrated.
3. The potential influence of chronic tonsillitis on male reproductive function may be mediated directly through systemic inflammation, oxidative stress, disruption of the blood–testis barrier, impairment of Sertoli and Leydig cell function, altered steroidogenesis and spermatogenesis, and indirectly through chronic prostatic inflammation.
4. The proposed pathophysiological model should be regarded as a testable hypothesis rather than an established causal relationship. Validation of this model requires prospective studies with simultaneous assessment of chronic tonsillitis, prostate status, semen parameters, reproductive hormone profiles, systemic inflammation and oxidative stress markers, as well as molecular comparison of the microbiota of tonsillar crypts, prostatic secretions, and seminal fluid.

DISCLOSURE

Author Contributions

Conceptualization: Viktor Paramonov, Lev Vysotskiy. Methodology: Viktor Paramonov, Lev Vysotskiy, Egor Paramonov. Writing – original draft: Viktor Paramonov, Artem

Albutov. Writing - review and editing: Viktor Paramonov, Artem Albutov. Visualization: Egor Paramonov, Pavel Shchennikov. Supervision: Alexander Derevyanov, Egor Paramonov, Yuriy Emelyanov. Literature search and selection: all authors.

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AI was used only as an auxiliary tool to support the literature search and language editing. All references, scientific interpretations, conclusions, and the final version of the manuscript were independently checked and approved by the authors. The authors accept full responsibility for the scientific content and final wording of the manuscript.

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