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	GUT MICROBIOTA AND RECURRENT UPPER RESPIRATORY TRACT INFECTIONS: EMERGING IMPLICATIONS FOR OTOLARYNGOLOGY
DOI	https://doi.org/10.31435/ijitss.3(51).2026.5782
RECEIVED	10 May 2026
ACCEPTED	15 August 2026
PUBLISHED	31 August 2026
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GUT MICROBIOTA AND RECURRENT UPPER RESPIRATORY TRACT INFECTIONS: EMERGING IMPLICATIONS FOR OTOLARYNGOLOGY

Wiktoria Pempuś *(Corresponding Author, Email: wikpem@gmail.com)*
Saint Queen Jadwiga Clinical Regional Hospital in Rzeszów, Rzeszów, Poland
ORCID ID: 0000-0002-5410-0766

Inga Jakubczyk
Saint Queen Jadwiga Clinical Regional Hospital in Rzeszów, Rzeszów, Poland
ORCID ID: 0009-0004-6982-3213

Kacper Szkodziński
University Clinical Hospital F. Chopin in Rzeszów, Rzeszów, Poland
ORCID ID: 0009-0009-1161-129X

Jagoda Maternia
Saint Queen Jadwiga Clinical Regional Hospital in Rzeszów, Rzeszów, Poland
ORCID ID: 0009-0000-9614-118X

Aleksandra Łoś
Saint Queen Jadwiga Clinical Regional Hospital in Rzeszów, Rzeszów, Poland
ORCID ID: 0009-0000-5094-1157

Karolina Majowicz-Czaszyńska
Saint Queen Jadwiga Clinical Regional Hospital in Rzeszów, Rzeszów, Poland
ORCID ID: 0009-0002-3240-8564

Nikola Król
Saint Queen Jadwiga Clinical Regional Hospital in Rzeszów, Rzeszów, Poland
ORCID ID: 0000-0002-5524-6476

Barbara Tomaszek
The Independent Public Healthcare Institution in Przeworsk, Przeworsk, Poland
ORCID ID: 0009-0001-8477-0007

Aleksanda Blok
The Independent Public Healthcare Institution in Przeworsk, Przeworsk, Poland
ORCID ID: 0009-0001-0813-0366

Dominik Wiater
University Clinical Hospital F. Chopin in Rzeszów, Rzeszów, Poland
ORCID ID: 0009-0005-3761-5118

Gabriela Płodzień
Saint Queen Jadwiga Clinical Regional Hospital in Rzeszów, Rzeszów, Poland
ORCID ID: 0009-0008-2193-9312

ABSTRACT

Recurrent upper respiratory tract infections (URTIs) represent a significant clinical challenge in otolaryngology, with growing evidence suggesting that intestinal microbiota may play an important role in their pathogenesis. The gut-lung axis describes bidirectional immunological, metabolic, and microbial communication between the gastrointestinal and respiratory systems. Disturbances in gut microbiota composition, known as dysbiosis, can impair mucosal immunity through altered IgA production, reduced regulatory T-cell activity, and decreased levels of immunomodulatory metabolites such as short-chain fatty acids. These changes may increase susceptibility to infections of the pharynx, sinuses, and middle ear, contributing to their chronic and recurrent course. Frequent antibiotic use, common in ENT practice, may further exacerbate dysbiosis, creating a potential vicious cycle of recurrent infections. Emerging therapeutic strategies - such as probiotics, prebiotics, dietary interventions, and personalized microbiome-based approaches - offer promising but yet insufficiently validated avenues for supporting standard treatment. Further prospective clinical studies are required to better define the role of the gut-lung axis in the development and management of recurrent ENT infections and to assess the effectiveness of microbiome-modulating therapies.

KEYWORDS

Gut–Lung Axis, Intestinal Dysbiosis, Microbiota, Recurrent ENT Infections, Mucosal Immunity, Probiotics

CITATION

Wiktoria Pempuś, Inga Jakubczyk, Kacper Szkodziński, Jagoda Maternia, Aleksandra Łoś, Karolina Majowicz-Czaszyńska, Nikola Król, Barbara Tomaszek, Aleksanda Blok, Dominik Wiater, Gabriela Płodzień. (2026). Gut Microbiota and Recurrent Upper Respiratory Tract Infections: Emerging Implications for Otolaryngology. *International Journal of Innovative Technologies in Social Science*. 3(51). doi: 10.31435/ijitss.3(51).2026.5782

Introduction

The gut microbiome constitutes a complex ecosystem of microorganisms that play a key role in maintaining the body's homeostasis. In recent years, its importance in modulating the immune response - both at the local and systemic level - has been increasingly emphasized. The interactions between the gut microbiota and the immune system influence susceptibility to infections as well as the course of many inflammatory diseases.

Particular attention has been drawn to the concept of the gut-lung axis, which posits the existence of bidirectional communication between the gastrointestinal tract and the respiratory system. The mechanisms underlying this interaction include modulation of the immune response by bacterial metabolites such as short-chain fatty acids, effects on T-cell function, and the regulation of inflammatory processes. An increasing body of research indicates that disturbances in the composition of the gut microbiota may lead to dysregulation of immune responses and heightened susceptibility to respiratory infections.

Upper respiratory tract infections are a significant clinical issue in otolaryngology due to their high prevalence and tendency to recur. The most common conditions include pharyngitis, sinusitis, and otitis media. Despite the widespread use of antibiotic therapy, some patients experience chronic or recurrent infections, suggesting the involvement of additional factors that influence immune system function.

Contemporary research increasingly focuses on the role of the microbiome in the pathogenesis of respiratory diseases; however, most available data concern the lower respiratory tract. Far less attention has been given to the relationship between the gut microbiota and upper respiratory tract infections relevant to otolaryngology. The immunological mechanisms responsible for the influence of gut dysbiosis on the recurrence of ENT infections, as well as the potential therapeutic opportunities arising from microbiome modulation, remain incompletely understood.

The aim of this paper is to present current knowledge on the role of the gut microbiome in the pathogenesis of recurrent upper respiratory tract infections and to discuss potential diagnostic and therapeutic implications for modern otolaryngology.

Gut microbiome and its role in immune regulation

The gut microbiome constitutes a complex ecosystem of microorganisms inhabiting the human gastrointestinal tract, comprising primarily bacteria but also viruses, fungi, and archaea. It is estimated that the number of microorganisms present in the gut is comparable to the total number of human cells, and their collective genetic material far exceeds that of the host. The dominant bacterial phyla found in the gastrointestinal tract are Firmicutes and Bacteroidetes, with smaller proportions of Proteobacteria, Actinobacteria, and Verrucomicrobia. The qualitative and quantitative composition of the gut microbiota is dynamic and depends on numerous factors, including mode of delivery, diet, age, lifestyle, environmental exposures, pharmacotherapy, and the course of previous infections.

Under physiological conditions, the gut microbiota remains in a state of equilibrium with the host organism, participating in numerous metabolic, protective, and immunological processes. One of the most important functions of the microbiome is maintaining the integrity of the intestinal barrier, which is a fundamental element of protection against the translocation of microorganisms and toxins into the systemic circulation. Gut microbes influence the tightness of intercellular junctions in the intestinal epithelium and stimulate the production of mucus and antimicrobial peptides.

Increasing attention is being paid to the role of the gut microbiota in modulating the immune response. The gastrointestinal tract is the largest immunological organ in the human body, and its mucosa is in constant contact with antigens originating both from the external environment and from commensal microorganisms. Interactions between the microbiota and the immune system are crucial for the maturation of immune cells and for maintaining balance between pro-inflammatory and anti-inflammatory responses.

Intestinal bacteria influence, among other processes, the activation of dendritic cells, the differentiation of T lymphocytes, and the production of cytokines. A particularly important role is attributed to regulatory T cells, which suppress excessive inflammatory responses and help maintain immune tolerance. The gut microbiota also contributes to the stimulation of immunoglobulin A (IgA) secretion, which plays a key role in mucosal immunity by neutralizing pathogens and limiting their adhesion to the epithelium.

A key mechanism through which the microbiome affects the immune system is the production of bacterial metabolites, primarily short-chain fatty acids (SCFAs) such as butyrate, propionate, and acetate. These compounds are produced during the fermentation of dietary fiber by gut bacteria and exhibit broad immunomodulatory effects. Short-chain fatty acids influence epithelial cell function, regulate macrophage activity, and promote the differentiation of regulatory T lymphocytes. Moreover, they exert anti-inflammatory effects by inhibiting the production of pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6.

Disturbance of the microbial balance within the gastrointestinal tract, known as dysbiosis, can lead to abnormal activation of the immune system and the development of chronic inflammation. Dysbiosis is characterized by reduced microbial diversity and an altered ratio between commensal and potentially pathogenic bacteria. The most common factors contributing to dysbiosis include improper diet, chronic stress, infections, and excessive or prolonged antibiotic therapy.

Although antibiotics are effective in treating bacterial infections, they can cause significant changes in the composition of the gut microbiota. The elimination of commensal bacteria promotes the overgrowth of opportunistic microorganisms and weakens mucosal immune mechanisms associated with the intestinal barrier. As a result, susceptibility to subsequent infections may increase, and chronic inflammatory activation may persist.

In recent years, it has been increasingly emphasized that the influence of the gut microbiota extends beyond the gastrointestinal tract and affects distant organs and systems, including the respiratory system. Immunological mechanisms linked to microbiome function can influence susceptibility to respiratory infections and the progression of inflammatory processes within the mucosa of the upper respiratory tract. This phenomenon forms the basis of the gut-lung axis concept, which has become the subject of intensive research in contemporary medicine.

Gut-lung axis

The gut-lung axis (GLA) is a concept describing the bidirectional communication between the gastrointestinal tract and the respiratory system. Despite the anatomical separation of these systems, numerous studies indicate the existence of complex immunological, metabolic, and microbiological connections between the gut and lung microbiota. These interactions play an important role in maintaining homeostasis and regulating immune responses.

The gut microbiota influences immune function through the production of bacterial metabolites such as short-chain fatty acids (SCFAs), modulation of regulatory T-cell activity, and regulation of both pro- and anti-inflammatory cytokine production. These metabolites can enter the systemic circulation and act on distant organs, including respiratory tissues. Consequently, the composition of the gut microbiota may affect susceptibility to respiratory infections and the progression of inflammatory processes.

A key component of the gut-lung axis involves the shared mucosal immune system. Immune activation within the gastrointestinal tract can influence defensive mechanisms in the respiratory epithelium through the migration of immune cells between mucosa-associated lymphoid tissues. Dysbiosis-disruption of the microbiota balance - may therefore lead to improper immune regulation and increased vulnerability to respiratory infections.

An increasing number of studies indicate that the gut-lung axis includes not only host-bacteria interactions but also the involvement of other microbiota components such as fungi and viruses. Interactions among these groups of microorganisms may shape inflammatory processes and affect the course of respiratory diseases. However, the underlying mechanisms remain insufficiently understood and are the subject of ongoing research.

Improved understanding of the relationships within the gut-lung axis may enable the development of new therapeutic strategies based on modulation of the gut microbiota. This may be particularly relevant for recurrent upper respiratory tract infections, in which dysregulated immune responses and chronic inflammation play an important pathogenic role.

ENT infections – characteristics and the problem of recurrence

Recurrent upper respiratory tract infections represent a significant clinical problem in otolaryngology due to their high prevalence, chronic nature, and strong tendency to recur. The most common conditions include pharyngitis, sinusitis, and otitis media. These disorders occur in both children and adults, negatively affecting quality of life and generating substantial diagnostic and therapeutic costs. Despite broad access to antibiotic therapy and modern treatment methods, some patients continue to experience persistent inflammation and increased susceptibility to subsequent infections.

Pharyngitis

Pharyngitis is one of the most common upper respiratory tract infections. Although viral etiologies predominate, bacterial infections - particularly those caused by Streptococcus pyogenes - also play a significant role. Clinical symptoms include sore throat, difficulty swallowing, fever, and enlargement of regional lymph nodes. In some patients, infections recur, contributing to chronic inflammation of the pharyngeal mucosa.

The pathogenesis of recurrent pharyngitis is complex and involves both environmental factors and disturbances in the host immune response. Increasing attention has been given to the role of bacterial biofilm, which enables microorganisms to persist on the mucosal surface and enhances their resistance to antibiotics. Prolonged or frequent antibiotic use may further disrupt the body's microbiota and weaken natural mucosal defense mechanisms.

Sinusitis

Sinusitis is another common condition in otolaryngology. Acute and chronic forms are distinguished, with the chronic form often associated with persistent mucosal inflammation and recurrent symptom exacerbations. Typical symptoms include nasal obstruction, nasal discharge, facial pain or pressure, and impaired sense of smell.

In recent years, growing emphasis has been placed on the local microbiome of the nose and paranasal sinuses. Under physiological conditions, microorganisms residing on mucosal surfaces help maintain immune balance and protect against pathogen colonization. Microbiota disturbances may lead to chronic inflammatory activation and increased susceptibility to infection. Additionally, bacterial biofilm hinders pathogen elimination and contributes to the chronic nature of the disease.

Frequent antibiotic use in patients with chronic or recurrent sinusitis remains a significant concern. Although short-term clinical improvement may occur, antibiotic therapy can further disrupt the microbiome and promote the selection of resistant bacterial strains.

Otitis media

Otitis media is one of the most common infectious diseases in childhood and a major reason for pediatric outpatient visits and antibiotic prescriptions. The condition typically develops due to bacterial or viral infections arising from eustachian tube dysfunction and preceding upper respiratory infections. Some patients experience recurrent episodes, potentially leading to hearing impairment and speech development delays in children.

Both anatomical and immunological factors play important roles in the development of recurrent infections. Increasing evidence suggests that impaired mucosal immunity and abnormal microbiota composition may influence susceptibility to otitis media. As with other ENT infections, frequent antibiotic use can disrupt microbial balance and sustain chronic inflammation.

Recurrent upper respiratory tract infections thus have a multifactorial etiology, involving not only direct pathogen effects but also disturbances in immune responses, the presence of bacterial biofilms, and changes in the body's microbiota. In recent years, it has been increasingly emphasized that gut dysbiosis may be one factor contributing to heightened susceptibility to ENT infections and their recurrent nature.

Intestinal dysbiosis as a potential factor in the recurrence of ENT infections

Intestinal dysbiosis, defined as a qualitative and quantitative imbalance of microorganisms inhabiting the gastrointestinal tract, can lead to significant alterations in host immune function. Growing evidence indicates that the gut microbiota plays a key role not only in maintaining gastrointestinal homeostasis but also in regulating immune responses in distant organs, including the upper respiratory tract. In this context, dysbiosis may represent one of the potential factors contributing to the recurrent nature of otolaryngological infections.

A healthy gut microbiota supports mucosal immunity by stimulating the production of immunoglobulin A (IgA), which plays a central role in neutralizing pathogens on mucosal surfaces. Commensal microorganisms also influence the differentiation of regulatory T lymphocytes, responsible for maintaining balance between inflammatory responses and immune tolerance. Bacterial metabolites - particularly short-chain fatty acids - further modulate immune cell activity and exhibit anti-inflammatory properties.

Under dysbiotic conditions, these mechanisms become impaired, leading to weakened mucosal immunity and increased susceptibility to infection. Reduced numbers of commensal bacteria and decreased microbial diversity result in dysregulated immune responses and promote low-grade chronic inflammation. Such an environment may facilitate pathogen colonization and hinder effective microbial clearance. Antibiotic therapy, widely used in treating upper respiratory tract infections, is a significant factor contributing to dysbiosis. Although effective in eliminating bacterial pathogens, antibiotics can induce unfavorable shifts in the gut microbiota, including a reduction in beneficial commensals and selection of opportunistic strains. Repeated cycles of infection and antibiotic treatment may create a vicious cycle in which microbiota disruption predisposes patients to further infectious episodes.

In the context of the upper respiratory tract, gut dysbiosis may be particularly relevant for mucosal immunity in the nose, pharynx, and middle ear. Disruption of the gut-lung axis may lead to abnormal immune regulation within these regions, increasing susceptibility to recurrent infections. Although these mechanisms are not yet fully understood, available evidence suggests that the gut microbiota may play an important role in the pathogenesis of chronic and recurrent ENT diseases.

Therefore, intestinal dysbiosis can be considered a potential modifier of both the course and recurrence of upper respiratory tract infections. Further research is needed to clarify the mechanisms underlying this relationship and to evaluate therapeutic opportunities arising from modulation of the gut microbiota in the context of ENT disorders.

Potential therapeutic strategies

Growing interest in the role of the gut microbiota in the pathogenesis of respiratory diseases has opened new therapeutic perspectives focused on modulating microbiome composition. In this context, interventions aimed at restoring microbial balance are increasingly considered as supportive measures in the prevention and treatment of upper respiratory tract infections. The most frequently discussed strategies include the use of probiotics and prebiotics, dietary modification, and future microbiome-targeted therapies.

Probiotics and prebiotics

Probiotics - defined as live microorganisms that, when administered in adequate amounts, confer health benefits to the host - are among the most extensively studied interventions affecting the gut microbiota. Their potential actions include modulation of immune responses, such as increasing immunoglobulin A production, regulating T-cell activity, and influencing the balance of pro- and anti-inflammatory cytokines. In the context of upper respiratory tract infections, it has been suggested that probiotics may reduce infection frequency by strengthening mucosal immunity.

Prebiotics, non-digestible food components that selectively stimulate the growth and activity of beneficial gut bacteria, may also play a significant role in microbiota modulation. By supporting the development of bacteria that produce short-chain fatty acids, prebiotics can indirectly influence immune function. Despite promising experimental findings, clinical data on the effectiveness of probiotics and prebiotics in the prevention of ENT infections remain inconclusive and require further investigation.

Diet and lifestyle

Diet is a key factor shaping the gut microbiota. A diet rich in dietary fiber promotes the production of short-chain fatty acids by gut bacteria, which may exert anti-inflammatory and immunomodulatory effects. Conversely, a low-fiber diet high in processed foods may reduce microbial diversity and promote dysbiosis.

Within the framework of the gut-lung axis, lifestyle factors such as physical activity, sleep quality, and stress exposure are also important. These factors can influence both gut microbiota composition and immune function, potentially modulating susceptibility to upper respiratory tract infections. Rational antibiotic use remains critical, as excessive use may cause long-term microbiota disturbances and increase vulnerability to recurrent infections.

Future therapeutic directions

Advances in microbiome research suggest the possibility of developing more advanced, personalized therapeutic strategies aimed at targeted microbiota modulation. Potential avenues include therapies based on precise manipulation of microbiome composition, the use of selected bacterial strains with immunomodulatory properties, and interventions targeting bacterial metabolites.

There is also growing interest in personalized medicine, in which a patient's microbiota profile could serve as an element in disease risk assessment and individualized therapeutic planning. In the context of recurrent upper respiratory tract infections, modulation of the gut microbiota may in the future become a valuable complement to standard treatments, particularly in patients prone to chronic or recurrent infections.

Despite promising prospects, most available data remain preliminary, and the effectiveness of many interventions requires confirmation in well-designed clinical trials. Therefore, at present, microbiome-oriented strategies should be considered as potential supportive approaches rather than primary methods in the treatment of otolaryngological infections.

Discussion

The presented data indicate a significant and multi-layered relationship between the gut microbiota and respiratory system function, a connection reflected in the concept of the gut–lung axis. An increasing number of studies suggest that disturbances in the composition of the gut microbiota may modulate immune responses and thereby increase susceptibility to upper respiratory tract infections. In otolaryngology, this may represent an important yet still under-recognized element in the pathogenesis of recurrent infections.

One of the key issues discussed in the literature is the nonspecific nature of the mechanisms linking intestinal dysbiosis with respiratory diseases. Although immunological and metabolic connections between the gut microbiota and the respiratory system have been demonstrated, most available data are indirect or derived from experimental studies. This means that the precise mechanisms through which the gut microbiota influences recurrent upper respiratory tract infections remain incompletely understood.

Another limitation of current research is methodological heterogeneity. Differences in microbiome analysis techniques, study populations, and clinical definitions of infection make it difficult to compare results and draw clear clinical conclusions. Long-term studies assessing the impact of gut microbiota changes on the frequency and course of ENT infections in a prospective manner are particularly lacking.

It is also important to note that most existing studies focus on the lower respiratory tract, in conditions such as asthma or chronic obstructive pulmonary disease, while upper respiratory infections remain relatively

understudied. Therefore, extrapolating gut-lung axis findings to otolaryngological conditions requires caution and further validation.

Despite these limitations, the concept of gut microbiota influencing the course of ENT infections is biologically plausible. Immunological mechanisms - such as regulation of inflammatory responses, the role of regulatory T lymphocytes, and IgA production - provide a coherent framework for understanding potential links between dysbiosis and increased infection susceptibility. The growing recognition of bacterial metabolites, particularly short-chain fatty acids, further highlights the microbiota's importance in maintaining immune homeostasis.

From a clinical perspective, potential therapeutic strategies based on modulation of the gut microbiota appear particularly promising. Although current evidence regarding the effectiveness of probiotics and other microbiome-targeted interventions in preventing ENT infections is limited and inconsistent, this direction represents an important area for future research. It may eventually lead to the development of novel supportive strategies for managing patients with recurrent upper respiratory tract infections.

In summary, the gut-lung axis represents a dynamic and rapidly developing field of research with potential relevance for otolaryngology. However, current knowledge does not yet allow for full translation of experimental observations into clinical practice, underscoring the need for further studies in this area.

Conclusions

The gut-lung axis represents an important communication pathway between the gastrointestinal and respiratory systems, grounded in immunological, metabolic, and microbiological interactions.

The gut microbiota plays a key role in regulating mucosal immunity, including effects on immunoglobulin A production, regulatory T-cell activity, and the generation of immunomodulatory metabolites.

Intestinal dysbiosis can disrupt immunological homeostasis, potentially increasing susceptibility to upper respiratory tract infections and contributing to their recurrent nature.

Recurrent otolaryngological infections - such as pharyngitis, sinusitis, and otitis media - have a multifactorial etiology, but disturbances in the microbiota are increasingly recognized as a possible component of their pathogenesis.

There is a likely relationship between antibiotic use, disruption of the gut microbiota, and increased frequency of upper respiratory infections, potentially creating a self-perpetuating cycle.

Microbiome-targeted interventions, including probiotics, prebiotics, and dietary modifications, represent a promising but still insufficiently validated approach to prevention and adjunctive treatment.

Further prospective clinical studies are needed to clarify the role of the gut-lung axis in the pathogenesis and management of otolaryngological infections and to assess the effectiveness of microbiome-modulating therapies.

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