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Breathe Easy: Unlocking the Power of Probiotics for Recurrent Respiratory Infections (RRIs) in Children

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Abstract:

Recurrent Respiratory Infections (RRIs) constitute a remarkable strength analysis and are liable for a serious mortality rate in children worldwide. Viral or bacterial infections have been recognized as vital contributing factors for death and disorder in the respiratory tract. Respiratory tract infections (RTIs) produce serious respiratory illnesses from common cold-like symptoms to severe conditions, usually attacking the lungs and other internal organs. Anyhow, RRIs particularly diminish a child or family's standard of living and give rise to therapeutic costs. Innate and acquired immunity are quickly involved in identifying and eliminating pathogenic species. Several nutritional additives like probiotics have been revealed to control immune functions and reduce the chance of RTIs. Probiotic bacteria as useful microbes can modify common viral replication, such as barrier functions and innate or adaptive immune responses. Moreover, interference with probiotics could influence the framework of the gut microbiota that can control pulmonary immune functions through the gut-lung axis. Hence, probiotics could guide medical management in designing targeted and alternative medicinal applications for RRIs in children

Keywords: *Respiratory tract infections (RTI), Recurrent Respiratory Infections (RRIs), Probiotics*

Introduction

Respiratory infections are repeated or chronic disorders, as one of the vital problems in children, having remarkable mortality (Troeger et al., 2018). Recurrent respiratory infections (RRIs) are a widespread health problem that gives rise to several doctor visits and regular professional care during childhood (de Oliveira et al., 2019). This has a major effect on the background of affected children, pediatricians, and the pharmaceutical labor (Nagaraju et al., 2021).

Moderate imperfection of the immune system, premature entry into nursery school, contamination in an environment, introduction to passive smoking,
or allergic conditions are some risk factors that lead to the reappearance of RRIs (Cuppari et al., 2020). Viral infections are significant for performing a vital role as a

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universal cause of respiratory infections (Charlton et al., 2018). The task of physicians and other healthcare contributors has been extended from simply curing disease to carrying out measures meant for health improvement or defense against disease (Organization, 2023).

However, antibiotics or anti-inflammatory medicines are often and inefficiently delivered in clinical applications. In this way, to minimize the inappropriate use of antibiotics, some other therapies have newly been suggested to lessen drug resistance and prohibit RRIs (Guitor & Wright, 2018). The survey of the nasal microbiome has led to the awareness of an application that utilizes "health-friendly bacteria" (Konovalovas et al., 2024). These bacteria activate immune responses or destroy harmful species by interchanging with the local epithelium and immune cells (Ranjha et al., 2021).

These bacteria turned out to be essential or productive microbes, commonly called probiotics, that help microbiome homeostasis as effective protection against the production of RRIs or in the analysis of some other infections such as Otitis media, SARS-CoV-2 infection, etc., (Cristiana et al., 2024). Probiotics have been appeared to be favorable for protecting or curing respiratory infections in an extreme population (Stavropoulou & Bezirtzoglou, 2020). This review focuses on an advanced research valuable discovery, allowing an understanding of the complex motility of RRIs or analyzing the prospects of probiotics as an established term to minimize the strength of these respiratory infections.

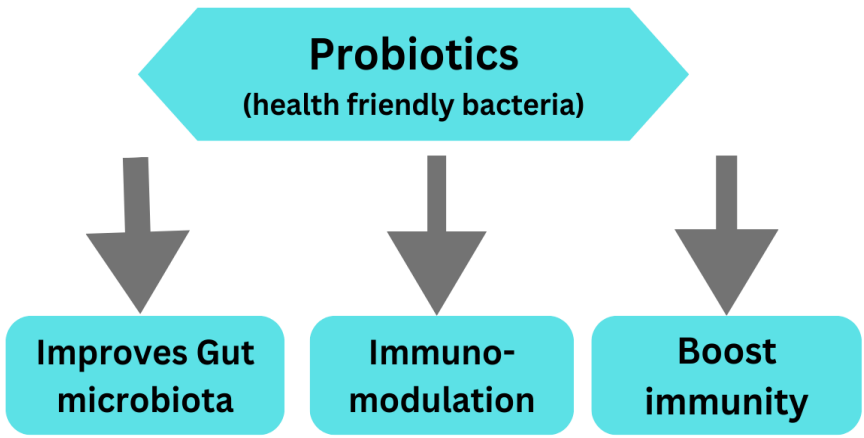
Outline of Recurrent Respiratory Infections (RRIs) and Probiotics:

Recurrent Respiratory Infections (RRIs) are a prevalent and universal medical situation, having a major general or economic effect, especially in children (Vysochyna & Kramarchuk, 2023). In 2020, to command doctors in the administration and protection of children with RRIs, an Italian inter-company agreement paper appeared to produce the latest definition of RRIs by analyzing international technical publications utilizing the GRADE method (Grading of Recommendations Assessment, Development, and Evaluation). It has been illustrated that in the first 6 years of age group, a child who did not undergo any clinical disorder encounters various RRIs that are usually lenient (Cristiana et al., 2024). Regardless of being a benign situation that is natural to get better by the age of 12 slowly, it particularly influences the child's safety and raises serious therapeutic costs (Chiappini et al., 2021).

In compliance with an updated definition of the International Scientific Association for Probiotics and Prebiotics (ISAPP), probiotic products are recommended as medical or protective choices for childhood disorders and produce biological organisms that impart beneficial health impacts on the host when consumed

adequately (D'Agostin et al., 2021). The human microbiome is a topic of important analysis interest, as well as its contribution to host preservation, biology, or the growth of a balanced immune system (Dominguez-Bello et al., 2019). Some probiotic strains have recently increased the relevant microbiota composition to avoid recurrent upper respiratory tract disorders (Debnath et al., 2022). These strains involve *Lactobacillus salivarius PS7, Streptococcus salivarius K12,* and *Streptococcus salivarius 24SMB*. Probiotics display strain-specific immunomodulatory effects on the immune cells and the host by triggering toll-like receptors (TLRs), likewise activating interferon (IFN) pathways (Raheem et al., 2021). Probiotic additives that improve the microbiota to provide healthiness have been expanding, bringing about the international operation of various probiotics in public and health maintenance environments (Kouhounde et al., 2022).

Figure 6: *Main Functions of Probiotics for Human Health*



Utilization of Probiotics in the Treatment of Respiratory Tract Infections:

RTIs are broadly generated by the development and disruption of various viral or bacterial microbes that may cause serious harm to the upper respiratory tract, for example, Influenza virus (IFV), enterovirus, adenovirus, and a respiratory syncytial virus are responsible for most respiratory disorders (Debnath et al., 2022). Recent research has illustrated that children with balanced immunity are less likely to develop respiratory microbes and their healing rate is faster (Govers et al., 2022). Probiotics have been investigated as a possible medical procedure to control entirely immune functions against several RTIs such as cough, pneumonia, asthma, pharyngitis, and laryngitis (Pico-Monllor et al., 2021). Probiotics are usually utilized orally as dietary

additives and food, e.g., yogurt. Hence, their main action site is in the gastrointestinal (GI) tract, which is subjected to pathogens or nutrients because of the thin mucosal layer (Lehtoranta et al., 2020).

The ability of probiotics is acknowledged as usable microbes that regulate the level of the favorable bacterial population in the gastrointestinal tract and boost host protection (Kerry et al., 2018). Probiotics also protect against other respiratory illnesses such as allergic reactions, chronic COPD, or inflammation in the airways by improving respiratory immunity (Huang et al., 2022). Probiotics can influence Treg cells, which are involved in eliminating allergic reactions (Dargahi et al., 2019). Recently, the *Bifidobacterium* or *Lactobacillus* probiotic combination utilized in this case is well-regulated to diminish the seriousness of many RRIs by increasing the possibility of a cure rate (Cristiana et al., 2024).

Table 4: *List of Some Probiotic Species with their Immunomodulatory Effects*

Probiotic species	**Immunomodulatory effects**
Streptococcus salivarius 24SMBc	Eliminates recurrent upper respiratory tract infections (URTIs) by rebalancing the nasal microbiota (Vertillo Aluisio et al., 2022).
Streptococcus oralis 89a	Particularly reduces the chances of symptoms in children suffering from RRIs by eliminating pathogens (Bidossi et al., 2018).
Lactobacillus Acidophilus	Regulate inflammatory disorders, boost barrier activities, and improve immunity (Gao et al., 2022).
Lactobacillus rhamnosus GG (LGG)	Trigger antigen-presenting cells (APCs) of healthy blood donors to increase immune responses (Fong et al., 2016).
Lactobacillus reuteri	Regulates the innate immune-cell response against microbes which shows anti-inflammatory activities (Kiššová et al., 2022).
Lactobacillus casei strains Shirota (LcS) and *DN114001*	Exhibits favorable impacts against various bacterial or viral contamination through the adjustment of immune homeostasis (Al Kassaa & AL KASSAA, 2017).
Lactobacillus salivarius AH102	Displays dose-dependent immunomodulatory effects on human dendritic cells (DCs) preventing airway infections such as asthma (Debnath et al., 2022).

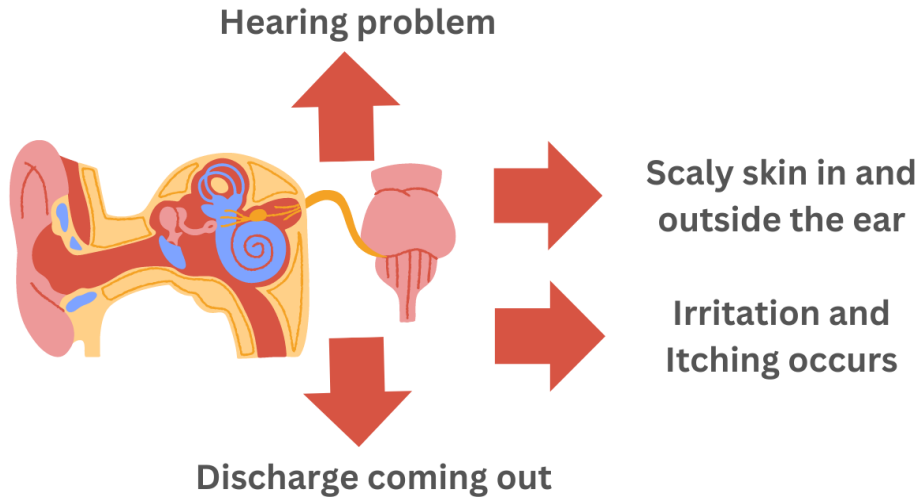
Streptococcus thermophilus	Improves regulatory DCs, and influences Treg cells against allergic reactions (Dargahi et al., 2021).
Bifidobacterium bifidum	Modify the immune system by enhancing immunoglobulins, triggering less epithelial breakdown of intestinal tissue (Lim & Shin, 2020).
Bifidobacterium breve AH1205	Prevention against allergic infections, and improves Treg activity by producing anti-inflammatory cytokines (Debnath et al., 2022).
Bifidobacterium longum AH1206	Promotes T-cells to prevent respiratory allergic infections, and maintains the balance of gut microbiota (Konieczna et al., 2012).

Treatment of Otitis Media in Children by Probiotics:

Acute otitis media (AOM) is the most common disorder in children linked with Eustachian tube dysfunction during upper respiratory tract infections, empowering pathogens to produce infection in the middle ear (Sarlin et al., 2023). General pathogens involve Streptococcus pneumonia, non-typeable Hemophilus influenzae (NTHi), and Moraxella catarrhalis, which increase rapidly in the nasopharynx (NP), where they reach the eustachian tube and produce OM (Browne, 2017). Therefore, persistent or improper utilization of antibiotics is linked with antimicrobial resistance and also enables expansion with resistant pathogenic strains (Romandini et al., 2021).

Treatment of AOM plays an important role in decreasing the complete usage of antibiotics in children (Suzuki et al., 2020). The management of probiotics has been analyzed to determine their capability to cure and reduce OM in children (Coleman & Cervin, 2019). *Lactobacillus* has mainly proven non-successful in curing AOM, which principally relates to the gut microbiome and only occupies the nasopharyngeal microbiome. Lately, economically convenient probiotic oral products producing *Streptococcus salivarius K12* strains may eliminate the comparative presence of pathogens in the nasopharyngeal microbiome while sustaining its biodiversity (Chen, 2021).

Figure 7: *General Complications of Ear Infections in Acute Otitis Media (AOM) in Children*

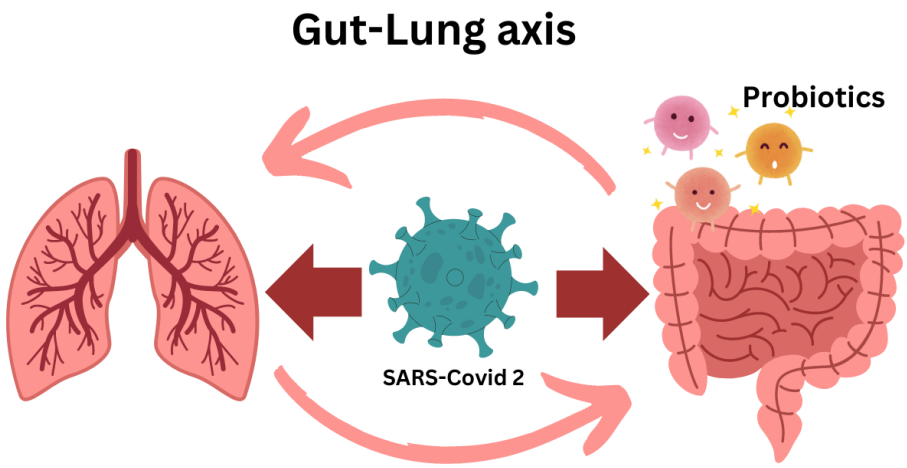


Treatment of SARS-CoV-2 infection in Children by Probiotics:

SARS-CoV-2 infection can exert both acute and chronic disorders, classified by an injury of tissue with a stimulated inflammatory reaction that is displayed in both respiratory tissues or systemic tissues, distal to the lungs (Iwasaki et al., 2021). With the development of a gut-lung axis of viral inflammation, the stability of the intestinal microbiome may play a major role in immune functions beyond virus-induced immunopathology (Tomkinson et al., 2023). The present research reported gastrointestinal (GI) features with diarrhea, inflammatory bowel disorders (IBD) with colitis, and a high ratio of deaths. It illustrates that dysbiosis mainly develops during SARS-CoV-2 infection because the gut-lung axis cannot be skipped (Ahlawat & Sharma, 2020).

Probiotics might aid in reducing inflammatory reactions of viral pathogenesis and respiratory symptoms by nourishing the host immunity or increasing the gut barrier systems. The probiotic strains such as *L. plantarum*, *lactobacillus rhamnosus*, *B. longum*, *L. bulgaricus*, *S. thermophilus*, and *D. pigrum* attack the respiratory tract through the gut-lung axis, enhance the immunity against SARS-CoV-2 infection as well as defeat the coronavirus infectious disorder-19 (COVID-19) epidemic (Cristiana et al., 2024).

Figure 8: *Schematic Diagram of Probiotics Gut-lung Axis to Protect against SARS-CoV-2 in a Pandemic*



Conclusion:

Probiotics have been proven successful for immune function modulation in preventing the replication of several viral respiratory diseases. The gut microbiome plays an effective role in health or disorder. The advantage of specific probiotic strains for controlling or inhibiting affected pediatric problems has been illustrated. In vitro analysis shows that probiotics have strain-specific immunomodulatory effects on the host or immune cells that trigger IFN pathways. The activation of the IFN pathways functions as the first line of defense against viral infections such as influenza virus, etc. Anyhow, an advanced study will provide extensive applications for combining probiotics into the prevention of recurrent respiratory infections (RRIs).

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