

Allergies and the microbiome

The microbiome plays an important role in the regulation of the immune system, and probiotics represent an interesting therapeutic option



2 CLINICAL STUDIES

- 8 weeks
- parallel
- randomized
- double-blinded
- placebo-controlled
- on 40 children patients and 40 adult patients

A targeted combination of 6 immuno-modulating probiotic strains

Allergies are occurring more and more frequently worldwide and represent a significant health problem.(1) In infants and young children, eczema is often the first symptom of an allergy. An allergy predisposition can then develop from a mild skin disorder to a food allergy, allergic rhinitis or asthma.



In the first study, researchers at two universities investigated the effect of this targeted combination of probiotic strains on atopic eczema.(24) Children in the intervention group between the ages of 1 and 13 had significantly reduced manifestations of atopic dermatitis compared to the placebo group. In addition, the occurrence of pro-inflammatory indicators was significantly reduced.

A second study, conducted at Griffith University, Australia, investigated the effect of this targeted combination of probiotics strains for allergic rhinitis. (14) This phase II study on 40 adults demonstrated the importance of the intervention approach, as there was a limitation of symptoms and an increase in the quality of life in the majority of persons.

The microbiome controls immunity

Allergies can have a serious impact on the patient's quality of life due to sleep problems, inability to perform daily and/or sports activities, and frequent absences from school or work.(2)

The most common allergies in Western countries are **eczema, hay fever (allergic)** and **asthma**. In recent years, there has been a particularly rapid increase in the prevalence of allergic disorders.(3)

Worldwide, **atopic eczema affects 15-30% of children** and **2-10% of adults, while allergic rhinitis occurs in 10-20% of the population.** (5)

However, the available treatment options for allergic conditions are limited, and treatment is generally aimed at alleviating symptoms. In recent years, scientists have made efforts to identify new ways to treat and prevent allergic conditions. Since **the gut microbiome plays an important role in the regulation of the immune system, probiotics represent an interesting therapeutic option.**

Significant changes in microbial exposure in the second half of the 20th century are thought to trigger the accelerating increase in allergic diseases.

Recent scientific studies have shown positive results of using probiotics as an adjunctive therapy for allergic conditions such as eczema and hay fever.

Allergy and the immune system

If the body's immune system shows a hypersensitive reaction to an otherwise harmless material (food, pollen, mold, mites, etc.) - an allergen, we speak of an allergy. When the body first encounters an allergen, it generally does not lead to an overreaction; in most cases this causes the production of immunoglobulin E (IgE). This process is called allergic sensitization.

Every time the body comes into contact with an allergen, the production of IgE causes the mast cells to start producing histamine. This histamine causes the symptoms of an allergic reaction. The more histamine is released, the more severe the symptoms. The amount of allergen, frequency and duration of exposure are also important factors in the development of allergy.(6)

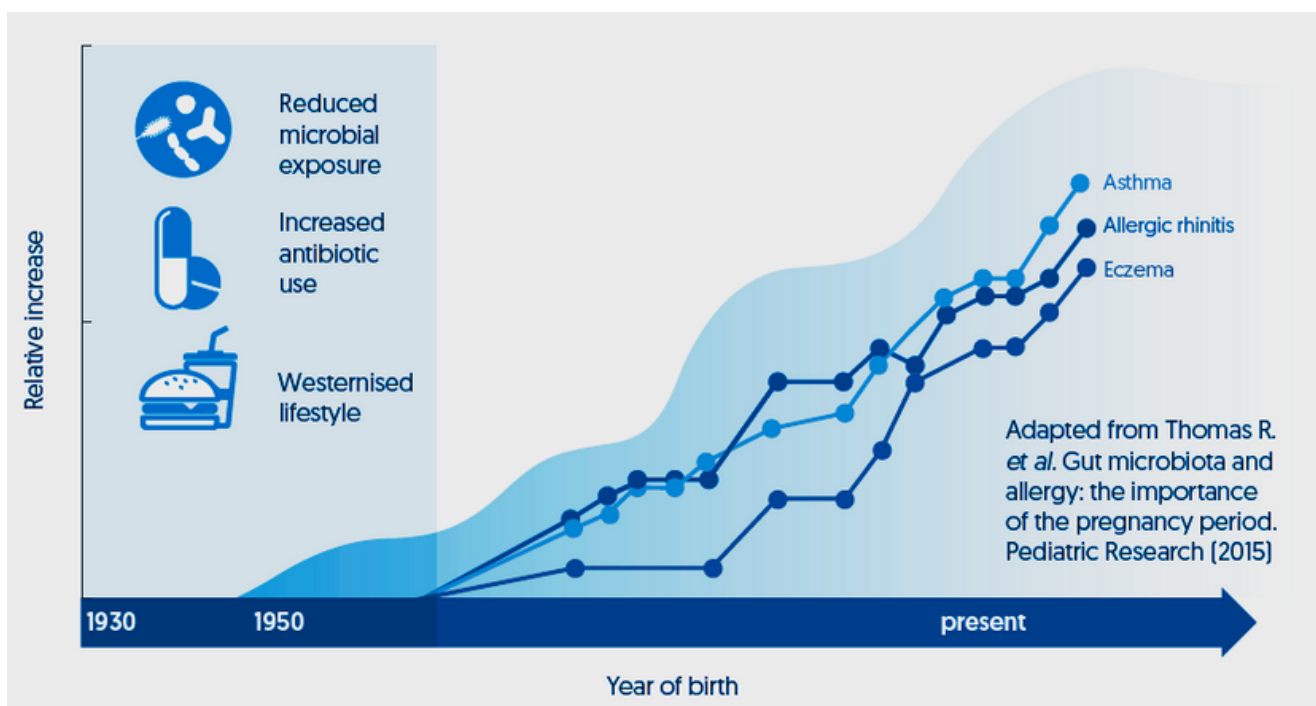


Figure 1. Increase in allergic diseases in the second half of the 20th century

Disturbed balance

Different types of white blood cells, which are part of the immune system, are involved in the allergic reaction. One of these cell types is the helper T-cell (Th), which plays a key role in allergy. There are several types of helper T cells, including Th1 and Th2 cells, which produce certain cytokines (including interleukins) during an immune response such as allergy.

Under normal conditions, the body maintains a certain **balance between the levels of Th1 and Th2 cells**. However, during an allergic reaction, this balance is disrupted, leading to excessive levels of Th2 cells. This subsequently causes **an increased production of the pro-inflammatory cytokines** IL-4, IL-5 and IL-13, which subsequently stimulate the production of IgE. IgE further causes **the release of histamine by mast cells**. Thus, Th cells and the cytokines they secrete are involved in the allergic reaction (7,8).



The course of allergy during life

There are different manifestations of allergy depending on the age of the person, which follow each other in a certain way. It is about the so-called "allergic march". **In infants and children, the allergy usually presents as eczema**. Children with eczema are more likely to develop other allergic diseases, such as **allergic rhinitis and asthma**, later in life.

In allergic rhinitis, an inflammatory reaction takes place on the mucous membranes of the nose, which results in **a runny nose, itching and sneezing**. It is also possible to feel **itching and burning of the eyes** (7). In about half of these cases, allergic rhinitis manifests itself as **"hay fever", that is, the allergy is a seasonal reaction** to tree and plant pollen. In the second half, allergic rhinitis represents **an allergy unrelated to the season**, e.g. allergy to dust mites or dander from cats, dogs or rodents (4).

Allergic rhinitis is closely related to asthma: about 40% of patients with allergic rhinitis also have asthma(9) and 80-90% of patients with allergic asthma also have allergic rhinitis. Difficulties can vary from mild to severe and can be random, intermittent or persistent.

The role of the gut microbiome

Various theories cite **the Western lifestyle, environmental factors and increased hygiene as possible causes of allergies**.

The hygiene hypothesis suggests that more allergies have appeared in recent decades because people have had limited contact with different microbes. (10) This hypothesis is currently being supplanted by new knowledge, where the composition and activity of the gut microbiome from birth significantly contributes to the occurrence of allergies. This fact points to **the essential role of the intestinal microbiome in the development of immunity. A great diversity of intestinal bacteria** is vital for the optimal function of the immune system. An unfavorable composition of the gut microbiome appears to play a role in the increase in hyperreactivity and inflammatory diseases, including allergic disorders.(9,11) Several studies have shown that **reduced diversity (dysbiosis) in the gut microbiome increases the risk of atopic eczema.**(12)

The role of the gut microbiome

In general, it is not possible to completely avoid allergens and treatment options for allergies are limited. Most treatments focus on symptom control and management. **Treatment with corticosteroid creams, antihistamines or other drugs is expensive, often reduces only part of the symptoms and can have unwanted side effects.**

In recent years, more and more attention has been paid to probiotics as a possible new therapy for allergies.(13)

Probiotics play a role in the regulation of the immune system and seem to have a beneficial effect on allergy symptoms. (14) This effect takes place at several levels, both within the intestine and throughout the organism. (15,16) Although the exact mechanisms are not yet known are fully elucidated, several hypotheses have been put forward to explain this effect. A number of studies have shown that therapy with specific probiotic strains leads to an improved balance between Th1 and Th2 cells, which **delays the onset of the inflammatory response after contact with an allergen.**(17,18)

Two systematic reviews with meta-analyses (19,20) provided an overview of existing studies (randomized controlled trials) on the effects of probiotics in people with allergic rhinitis, in which researchers compared different probiotics with placebo. The authors of both reviews concluded that, despite the heterogeneity of probiotics used, there is sufficient evidence to support the view that **probiotics can reduce the severity of symptoms and complications in people with allergic rhinitis and can improve their quality of life.**

Probiotics were also well tolerated by the research participants. Two other systematic reviews with meta-analyses(21, 22) also showed that **probiotics can significantly reduce the risk of eczema, especially in young children.**

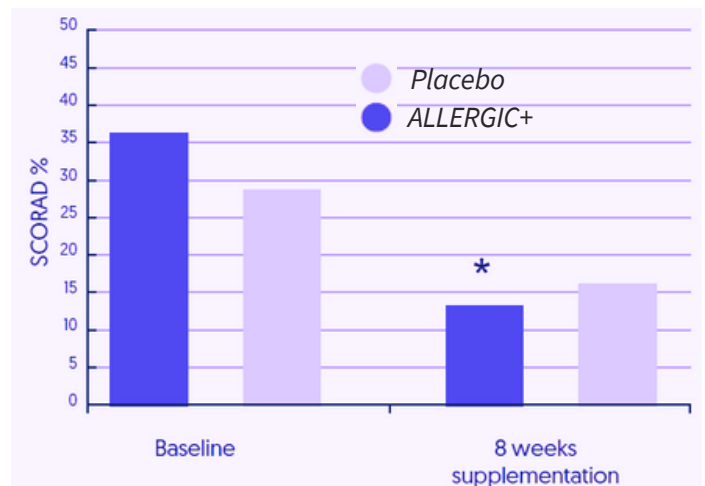


Figure 2. Changes in the SCORAD index before and after the intervention.

* Significant decrease, $p=0.005$

Atopic eczema

In a randomized controlled trial, researchers at two Turkish universities investigated the effect of this preparation on atopic eczema.(24)

Forty children aged 1 to 13 years with atopic eczema were given 2 g of a targeted probiotic (4×10 billion CFU/day) or a placebo twice daily. In addition to assessing their quality of life and severity of symptoms, the researchers performed tests to measure cytokine and IgE blood levels.

After eight weeks, children receiving the targeted probiotic showed **significantly reduced symptoms of atopic dermatitis** compared to the placebo group, see Figure 2.

The probiotic group also showed **significant reductions in levels of IL-5, IL-6 and IFN-alpha**, substances whose presence indicates an inflammatory response is underway. The same was true for IgE levels: children who received a targeted probiotic showed significantly lower blood levels than those who received a placebo.

Allergic rhinitis

A second study, conducted at Griffith University, Australia, investigated the effect of a targeted probiotic on allergic rhinitis.(14) This phase II study was designed according to the Simon two-stage plan.(13)

The goal of the two-stage plan is to determine whether the treatment has sufficient biological activity to warrant further development.

During the study, 40 adults with allergic rhinitis took 2 grams of a targeted probiotic twice daily (4 x 10 billion CFU/day) for eight weeks. During the study, participants reported their quality of life, **hay fever symptoms**, and use of other medications.

After four weeks, 50% of participants reported an improved quality of life, as measured by the "mini-rhinoconjunctivitis quality of life questionnaire" (mRQLQ). After eight weeks, this percentage increased to 63%, representing a statistically significant and **clinically relevant improvement in quality of life**, see Figure 3.

There was also a significant reduction in the total individual mRQLQ score as well as **symptoms affecting the eyes and nose** of the participants. **The use of other drugs also decreased.** The vast majority of patients tolerated the targeted probiotic well.

A targeted probiotic

- + reduces the risk of eczema
- + reduces the symptoms of hay fever
- + improves the quality of life

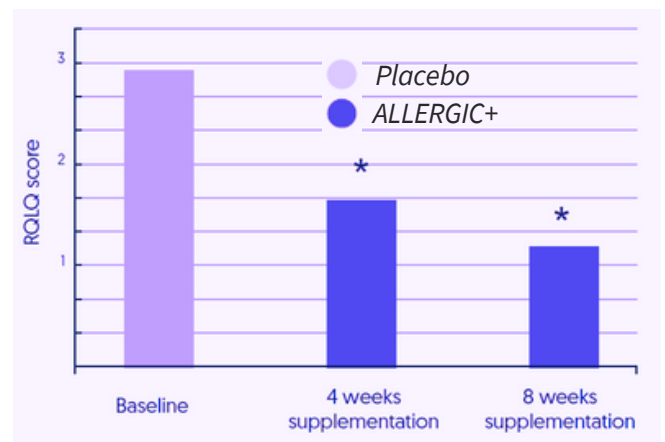


Figure 3. RQLQ scores before and after the intervention.

* Significant decrease, $p=0.005$

In patients suffering from allergic rhinitis, the severity of symptoms correlates only slightly with how patients feel. Therapy should therefore focus **not only on reducing symptoms, but also on reducing disorders that patients consider important** (e.g. increasing quality of life).

In the current study, a targeted probiotic was shown not only to **reduce hay fever symptoms**, but more importantly, to cause a clinically significant **improvement in quality of life**. The personal burden of the disease, as perceived by patients with hay fever, can be positively affected by the use of a targeted probiotic.

This information has not been evaluated by the Department of Health of the United Kingdom. Neither the information nor any formulas provided are intended to diagnose, treat, cure or prevent any disease.

ALLERGIC+ contains probiotic strains purposefully selected on the basis of scientific research and clinical studies aimed at monitoring the symptoms of allergy, asthma and eczema.

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