As the prevalence of atopic dermatitis (AD) increases, especially in developed countries and Western societies, affected individuals and those who treat them are interested in innovative approaches to symptom management.

Dysbiosis of the skin microbiota has implications for many of the skin disorders encountered in the clinic, including AD. Mounting evidence suggests the importance of a diverse microbiome for maintaining skin homeostasis, influencing metabolic processes, contributing to immunity, and an overall beneficial effect on skin health. It is debatable whether dysbiosis precedes or is a consequence of all skin disorders, though there is evidence that decreased diversity is apparent prior to atopic flares. However, overall, the evidence available suggests that rebalancing strategies may be broadly beneficial.

The potential to modulate the skin microbiome via topical product application suggests a tantalizingly simple approach to supporting skin health in individuals with skin symptoms associated with AD, including dryness, xerosis, and itch. Given the chronic nature of the condition, cost-efficient interventions are particularly attractive. And topical modulation of the cutaneous microbiota represents an attractive approach to patient care.

La Roche-Posay has been actively researching and conducting clinical studies to better understand the skin microbiome for 10 years. The company continues to fund research in efforts to enhance clinical knowledge and produce solutions that could have important benefits to support symptom management.

RETHINKING EMOllIENTS

Topical emollient products, either nonpharmacologic or prescription, are used as monotherapy or as adjuncts to other courses of therapy in AD to soften and moisturize the skin and possibly to help restore stratum corneum deficits that lead to disruption of barrier function. However, clinicians recognize that the quality and clinical effect of emollient formulations can vary significantly. In fact, some ingredients have been suggested to degrade the skin barrier, while others have been shown to offer barrier support. Recently, the potential to support a healthy skin microbiome via topical formulations has gained increased attention.

La Roche-Posay has pioneered research into topical modulation of the skin microbiome, with the goal to deliver rigorously proven, clinically beneficial products to help manage the symptoms of AD and reduce flares. Since 1905, thermal dermatology patients have visited the center in the town of La Roche-Posay, France for management of eczema and other skin disorders. Insurers in France currently cover these treatments for patients with AD, psoriasis, and related skin diseases. The history of successful skin improvement associated with bathing in the springs inspired the company La Roche-Posay to formulate at-home solutions for skin care, incorporating La Roche-Posay Thermal Spring water (LRP-TSW). The company has been dogged in its mission to understand how LRP-TSW confers benefits and to deliver that benefit in commercially available skincare.

LRP-TSW has a specific and unique mineral and bacterial fingerprint that is only found in the water from this particu-
Key Considerations: Understanding AD and Its Management

New and emerging data continue to reshape our understanding of atopic dermatitis, with important implications for patient care.

- Symptoms of AD—intense itching (which feels good to scratch), eczema in characteristic, symmetric locations, and chronicity—typically first appear in early childhood, but AD can persist into and even start in adulthood for a sizable population of patients.
- About 10% of adults develop AD during their lifetime.
- Emerging evidence links cutaneous dysbiosis to skin disease, a possible consideration in patient care.
- Supportive topical skincare is commonly used by individuals with AD to soften and moisturize the skin and relieve symptoms.
- Appropriately formulated skincare may restore skin deficits that disrupt the barrier.
- Topical emollients may address symptoms, such as dryness and itch.
- Clinicians should recommend formulations with anticipated benefits that patients will use in real-world settings.

Its unique composition can be associated with a proprietary ingredient called Aqua Posae Filiformis (APF), a biomass consisting of prebiotics, as well as postbiotic products. APF is a lysate of Vitreoscilla Filiformis grown in LRP-TSW containing medium with demonstrated benefits on inflammation and immunoregulation. Evidence suggests that LRP-TSW and APF formulations may have skin supportive benefits that help to rebalance the microbiome.

To date, LRP-TSW and APF-containing products have been tested in multiple clinical studies by LRP, which has the data on file, and which have been published in peer reviewed dermatology journals. These trials have been a blend of clinical and observational studies, with study endpoints dependent on an investigator evaluation and outcomes from patient self-reporting. Data are also available from studies evaluating LRP-TSW and APF-containing products used alone or in conjunction with what may be considered standard of care for AD, such as topical corticosteroids.

STUDY DATA

Real-world Benefit. Evidence supports the benefits of using LRP-TSW and APF-containing products—alone or with conventional therapeutics—to improve AD symptoms. Data from an international observational trial performed in 11 countries and involving 9,035 patients aged four days to 91 years with mild to moderate AD (five percent of patients had severe AD) provides a glimpse of how an emollient formulation containing LRP-TSW and APF might perform in a real world setting. Investigator-rated improvements in clinical outcomes were similar.

PATIENT SELF-ASSESSMENT

| Patients | I sleep better | 98% |
| I feel less stressed | 97% |
| I feel more confident | 98% |
| I feel less affected in my daily life | 98% |
| I have more time for my leisure activities | 95% |

| Parents | I feel less tired | 97% |
| I feel calmer | 99% |
| My daily life is improved | 98% |

| As a monotherapy | N=1370 |

Investigator Assessment:

Figure 1. QOL + Evaluation of Eczema Improvement and Tolerability - Monotherapy
when the formulation was used as a stand-alone intervention or when used along with standard therapeutic interventions for AD. Similarly, patient-reported improvements in quality of life metrics were similar whether the formulation was used as monotherapy or in combination therapy (Figures 1 and 2).

Reduction of prescription use. Another study—this time in 2,568 children aged one month to 18 years—suggests that use of the LRP-TSW and APF-containing emollient may allow for a reduction in use of corticosteroids and other treatments. A majority (83.4 percent) of 1,353 patients using a steroid were able to reduce the frequency of steroid use, and 71.5 percent of 907 users reduced antihistamine use (a boon given the use of antihistamines in AD is against current recommendations), once they added the emollient to their regimen.

Symptom improvement and flare reduction. A double blind study performed on two groups of 50 AD patients showed that one month after the end of an efficient therapeutic treatment, 84 percent of patients using an LRP-TSW and APF based emollient were in maintenance versus 61 percent for a comparator emollient. Furthermore, in case of relapse, the global worsening of SCORAD rates were 16 percent and 39 percent, respectively, with significantly less product use (192g versus 224g). As well, skin samples taken from subjects in each group demonstrated greater Staphylococcus reduction in the...
EMOLLIENT-BASED THERAPY FOR AD: A POTENTIAL ROLE FOR REBALANCING THE MICROBIOME

Product Focus

Lipikar Balm AP+

- Clinically shown to reduce dry, rough skin.
- Formulated with La Roche-Posay Prebiotic Thermal Water, Aqua Posae Filiformis, Shea Butter (20%), Glycerin (7%), and Niacinamide (4%).
- Quick absorbing formula in a creamy, comforting balm texture.
- Non-greasy and non-sticky finish.
- Suitable for babies two weeks and up, children and adults. Accepted by the National Eczema Association.
- Non-comedogenic.

Lipikar group compared to the reference emollient in both affected and unaffected skin areas. While these are small numbers of patients studied, they nevertheless suggest a benefit for strategies centered on rebalancing the skin microbiome to achieve more physiologic conditions.

Outcomes indicative of good compliance are important to note: 85 percent reported that LRP-TSW-based emollient moisturized all day long, 94 percent said it was easily spreadable, and 96 percent reported that the application was easy to use. As well, 89 percent had a reduced desire to scratch.

A separate evaluation that looked at tolerance and SCORAD reduction in 51 children and adults with moderate to severe AD showed that the LRP-TSW-based emollient notably reduced pruritus by day 14 (average 41 percent reduction) and was associated with improvement in sleep for 86 percent of subjects by day 14.

REBALANCING THE SKIN MICROBIOME: A PLASIBLE AD TREATMENT STRATEGY

The efficacy demonstrated by the LRP-TSW and APF-based emollient in accumulated studies may be explained in part by several unique biological impacts. Clinical studies have shown that topical LRP-TSW treatment has a prebiotic demonstrated activity, resulting in increases in Gram-negative bacteria and improvement in skin microbial diversity. In addition, in vitro testing on reconstructed epidermis, with APF demonstrated that it stimulated endogenous antioxidant and antimicrobial defenses.

Secondly, it may also contribute to rebalancing of the skin’s microbiome by supporting growth of beneficial commensal bacteria. There is evidence that treatment with LRP-TSW and/or APF may encourage propagation of the Xanthomonas genus of the Proteobacteria phylum, which paralleled clinically longer durations between AD flares and less severe ones. Interestingly, studies showed that as Xanthomonas population increased, Staphylococcus communities decreased.

CONCLUSION

The growing body of research on the role of dysbiosis in skin disease underscores the importance of choosing the proper topical emollient to manipulate the cutaneous microbiota for a given patient. No longer is the goal of topical emollients simply to soften the skin feel or prevent moisture loss. Rather, the prospect of rebalancing the skin microbiome through topical product application offers intriguing potential for the management of AD. Efforts to restore bacterial loads and diversity in affected skin areas appears to equip the human body (and perhaps the immune system) with a better chance of restoring damage and maintaining skin health.