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# **Examining Atopic Dermatitis Through the One Health Concept Lens**

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#### **ABSTRACT**

This paper explores the application of the One Health framework to atopic dermatitis (AD), a complex, chronic skin disease, emphasizing interdisciplinary approaches to prevention and management. One Health integrates human, animal, environmental, and plant health, addressing challenges such as antimicrobial resistance, infectious diseases, and neglected tropical diseases (NTDs). In the context of AD, One Health principles are applied to explore etiological factors like urbanization, climate change, biodiversity loss, and environmental pollution. Key findings include the interplay between lifestyle and environmental exposures, as evidenced by studies on human-dog microbiota sharing, which reveal that rural environments confer protective effects against allergic conditions for both species. Historical observations of the "old farm effect" highlight the protective role of traditional rural living, including raw milk consumption, in preventing atopic diseases. However, modern urbanization and industrial farming have eroded these benefits. Climate change intensifies AD symptoms through extreme weather, proliferation of more and higher allergenic pollen, likely also of house dust mites, allergen proliferation, and pollution. Rising CO<sub>2</sub> levels exacerbate pollen allergenicity, prolong pollen seasons, and amplify allergic responses. The skin's microbiome and immune barrier are sensitive to pollutants like black carbon and traffic-related emissions, further influencing AD prevalence and severity. Innovative approaches to prevention, such as veterinary vaccination strategies targeting allergens or immunopathological key cytokines, illustrate cross-species solutions. Web data mining demonstrates potential for analyzing public interest and seasonal trends in AD, correlating search data with real-time monitored environmental factors and highlighting gaps in awareness and access to modern treatments. This integrative One Health lens provides a framework for reimagining AD prevention and management, emphasizing a return to environmental and lifestyle diversity, climate action, and leveraging digital and biomedical tools for personalized, sustainable care.

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#### 1 | Introduction

This paper summarizes a symposium held by the International Society of Atopic Dermatitis on April 4, 2024. The One Health concept is an integrating and unifying approach to looking at health. It acknowledges the interconnectedness of human, animal, plant, and environmental health. It aims to optimize health care through interdisciplinary and intersectoral collaboration and to achieve a sustainable balance [1]. One Health involves tackling problems in a holistic way, moving away from curative medicine toward prevention and control by bringing together different disciplines and finding various facets of a problem. The One Health approach has been applied to multiple issues, including antimicrobial resistance, infectious diseases, vector-borne diseases, and foodborne diseases, which all involve the interconnectedness of human, animal, and environmental health [2]. The World Health Organization (WHO), the Food and Agriculture Organization (FAO), the World Organization for Animal Health (Office International des Épizooties OIE), and the United Nations Environmental Programme (UNEP) have come together to provide a global example of a way forward in tackling complex health issues through the One Health approach [3].

Neglected tropical diseases (NTDs), which are diseases of poverty affecting the most disenfranchised populations, have been looked at through a One Health lens, as these populations often share their environment closely with animals and live in the same shared space [4]. The WHO One Health approach in the context of NTDs and has recently been applied to skin entities. Skin NTDs are now uncommon among individuals who come to primary healthcare centers because of skin concerns [5]. Thus, including common chronic skin diseases like AD was an important move in WHO policy to promote skin health [6].

Some concepts central to this review include the exposome and the epithelial barrier theory (Box 1 and Figure 1), both of which are highly relevant to atopic dermatitis (AD). The exposome encompasses the totality of environmental exposures across a lifetime including diet, pollutants, microbes, climate, and psychosocial stressors—and offers a valuable framework for understanding how complex external factors such as urban pollution, allergens, and chemical exposures contribute to the development and exacerbation of AD [7]. When integrated into a One Health perspective, the exposome highlights how shared environments—such as those between pets and owners—can shape immune responses and promote inflammatory conditions. Complementing this, the epithelial barrier theory [8] posits that environmental insults can impair barrier integrity in the skin, gut, and lungs, leading to increased permeability, immune dysregulation, and heightened allergic disease risk [9]. AD exemplifies this mechanism, as skin barrier defects (e.g., filaggrin mutations) are linked to increased susceptibility to food allergy and asthma [10]. Framing both concepts within a One Health approach underscores the need for integrated strategies that address environmental, animal, and human health to prevent allergic diseases more effectively.

In this review, the One Health lens is considered to examine atopic dermatitis (AD), with the aim of exploring and inspiring change. AD, as a complex disease, requires a holistic approach to understand its root causes, considering its various etiological factors [11], and the One Health concept provides, theoretically, a unique

**BOX 1** | The epithelial barrier theory and the exposome.

- Core idea: Environmental stressors (pollutants, detergents, allergens) disrupt epithelial barriers in skin, lung, and gut—triggering inflammation and immune imbalance.
- Exposome connection: The totality of lifetime environmental exposures ("exposome") contributes to barrier dysfunction and chronic disease.
- AD implications: A damaged barrier allows allergen and microbe entry, setting off inflammatory cascades seen in atopic dermatitis.
- One Health extension: These disruptions are seen across species and ecosystems, supporting a unified model of chronic inflammatory disease origins.

combined approach to approaching this disease. Relevant examples pertaining to One Health in the context of AD and allergy were chosen, including the hygiene/loss of biodiversity hypothesis, the coexistence of AD in humans and pet dogs, why we lost the originally protective farm effect, the promotion of prevention of allergic diseases by vaccination in veterinary medicine, predictions/prevention of the impact of global warming on allergies, and web data mining to monitor and prevent AD and allergies. Some perspectives are proposed by the panel of convened specialists, with an emphasis on prevention and adaptation.

### 2 | One Health and AD Historical Starting Points: Hygiene, Climate Change, Pets, Urbanization, Pollution

The hygiene hypothesis [12] suggests that a lack of early childhood exposure of humans to infectious agents, microorganisms, and parasites leads to increased susceptibility to allergic and autoimmune diseases later in life. The biodiversity hypothesis [13] is an extension of the hygiene hypothesis, taking it a step further by considering the impact of environmental changes on human and animal health. Improved sanitation, reduced family size, and decreased exposure to infections in developed countries contribute to the rise of allergic conditions such as asthma or AD. However, conflicting evidence from urban environments—such as subways and malls—suggests that not just the presence, but the quality of exposure to infectious agents matters. In contrast, early exposure to a diverse range of microorganisms in settings like the "old farm" environment appears to support healthy immune system development and function [14].

Climate change affects AD, with extreme weather changes, humidity, and temperature fluctuations triggering symptoms in patients. High humidity can exacerbate AD symptoms, leading to sweating, moisture retention, itching, and inflammation, while extreme temperatures can aggravate the condition. UV radiation and sun exposure have both positive and negative effects on AD, with moderate exposure being beneficial but excessive exposure leading to skin damage and worsening AD. Climate influences the presence and distribution of allergens such as

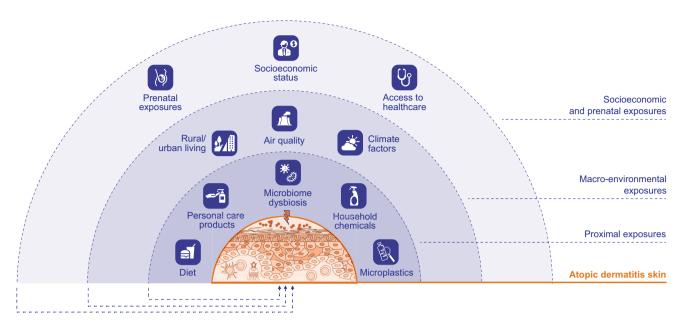


FIGURE 1 | Exposomic factors related to atopic dermatitis. A conceptual model illustrating the multilayered exposome contributing to AD pathogenesis. At the center is inflamed skin, representing the clinical manifestation of AD. Surrounding the core are concentric rings grouping exposomic factors by proximity and type: (1) the innermost ring includes proximal exposures such as skin microbiome dysbiosis (notably *Staphylococcus aureus* colonization), diet, and chemical exposures (e.g., personal care products, microplastics); (2) the middle ring represents macro-environmental factors, including air pollution, climate, and urban vs. rural living; (3) the outermost ring encompasses broader contextual exposures, such as socioeconomic status, access to healthcare, and early-life or prenatal exposures (e.g., maternal smoking, cesarean delivery). Arrows denote the cumulative and inward influence of these factors on human skin, highlighting the complex and dynamic nature of the exposome in AD pathophysiology.

pollen, mold, and dust, impacting people with AD, especially during seasonal changes [15–18].

Exposure to certain allergens, including pet dander, can exacerbate symptoms in individuals predisposed to AD, with proteins found in skin cells, urine, saliva, or fur of animals acting as triggers. However, living with a dog does not predispose individuals to atopic disease, but rather does the opposite, and more research is needed to understand this relationship [19]. Urban areas with polluted air have increased numbers of AD patients, and a large Korean cohort demonstrated that long-term exposure to air pollutants, including gases and particulate matter, is an independent risk factor for developing AD [20]. Figure 2 summarizes additional factors when considering AD through the One Health lens.

### 3 | Canine Atopic Dermatitis vs. Human Atopic Dermatitis

Pet dogs are considered valuable models for studying the impact of living environments on health, as they spend most of their time indoors with their owners. Contrary to cats, where none of the allergic skin diseases show features consistent with AD [21], canine atopic dermatitis is regarded as a highly relevant model for human AD [22] and Figure 3. Dogs have simpler lives than humans, living in close environments and developing quickly, making them suitable for research, but there is limited research on dog allergies—manifested most commonly as canine atopic dermatitis—and immunology, and

less control over medication use in dogs compared to humans. A study was conducted in southern Finland, focusing on two dog breeds: Labrador Retriever and Finnish Lapphund, collecting blood and skin microbiota samples from the dogs and their owners [23, 24]. The owners also filled out large questionnaires and collected fecal samples from themselves and their dogs. The study defined two lifestyle groups: urban and rural, with urban lifestyles characterized by dogs living with one person, having many hobbies, and living in apartment buildings, and rural lifestyles characterized by dogs living in big families with children and other pets. This distinction (rural/urban) was not necessarily related to the true physical environment, but rather to lifestyle factors such as living alone in a high-rise building or having a large family.

The study found that lifestyle and environmental factors influenced the composition of skin microbiota in dogs, with differences in the prevalence of allergic symptoms between dogs living in rural and urban environments. Dogs living in rural environments with a rural lifestyle were less likely to have allergic symptoms, while those living in urban environments with an urban lifestyle were more likely to have allergic symptoms. Allergic dogs were more likely to have allergic owners, and vice versa, suggesting that owners and dogs may be allergic or healthy together [23, 25]. Healthy dog-owner pairs were more likely to live in rural environments and have a rural lifestyle compared to allergic dog-owner pairs, who typically lived in urban environments. The microbiotas of humans and dogs were found to be dissimilar, particularly in terms of gut microbiota, likely due to differences in diet and skin function,

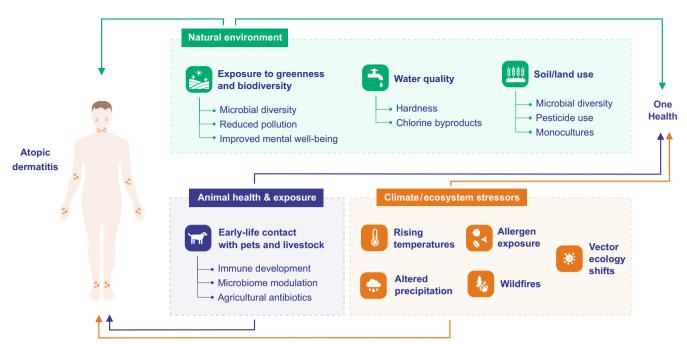


FIGURE 2 | One Health lens to examine AD. A One Health framework for understanding atopic dermatitis (AD) through interconnected environmental, animal, and ecosystem factors. This systems-based model illustrates how the human skin and immune system—central to AD risk—are influenced by interacting domains of the One Health triad. (1) Environmental ecosystem health, including exposure to greenness and biodiversity (linked to microbial diversity, reduced pollution, and stress modulation), water quality (e.g., hardness, chlorine byproducts), and soil/land use (influencing microbial exposure); (2) Animal and zoonotic interfaces, such as early-life contact with pets and livestock, which may shape immune development and skin microbiota, while agricultural antibiotic use may disrupt environmental microbial ecosystems; (3) Climate-linked stressors, including rising temperatures, allergen exposure, altered precipitation, wildfires, and shifts in vector ecology—all of which can aggravate AD via inflammatory and barrier-related pathways. Arrows and feedback loops emphasize the bidirectional influences and cumulative impact of environmental degradation on AD pathogenesis, highlighting the relevance of an integrative One Health perspective.

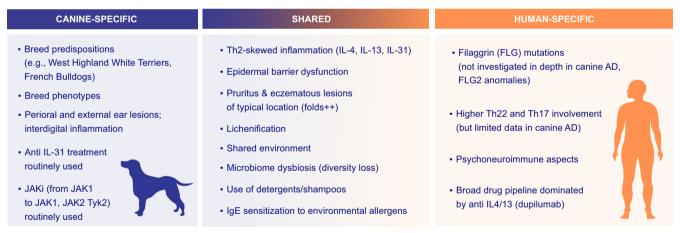


FIGURE 3 | Comparative features of atopic dermatitis in humans and dogs.

despite sharing homes and possibly diet. However, the skin microbiota of dogs and humans was found to be quite similar, with dog-owner pairs sharing a large proportion of skin microbes, suggesting that close connection increases the sharing of skin microbes. The similarity in skin microbiota between species suggests that if environmental microbes play a role in the development of diseases in both species, the effect is more likely to occur through the skin rather than the gut [23, 25]. Adding complexity to the influence of lifestyle and environment, recent research shows that dogs are directly affected by

their owners' emotional states. Specifically, dogs can detect and respond to the stress of unfamiliar humans through olfactory cues, which in turn can influence their cognitive bias responses [26]. Furthermore, urban living has been associated with negative effects on anxiety-related behaviors in dogs. A large-scale study found that urban environments—particularly when combined with inadequate socialization and low activity levels—are significantly linked to increased social fearfulness in pet dogs [27]. Overall, these findings support the view that both the owner's emotional state and the dog's

living environment are key factors influencing canine anxiety and stress-related behaviors. They may also contribute to the development of stress-linked conditions, such as atopic dermatitis.

### 4 | The "Old Farm" Effect Revisited: Consequences for Prevention

The traditional "old farm" lifestyle has been associated with a healthier immune phenotype, often referred to as the "farm effect" (Figure 4). Epidemiological studies have consistently shown that exposure to farm-related aerosols and the consumption of raw cow's milk are strongly protective against various atopic diseases, including atopic dermatitis [28, 31–33]. Historical awareness of these protective effects dates to the 19th century, when health resorts and sanatoriums were established near cowsheds in altitude regions such as Davos, Switzerland, or thermal sites such as Bad

Gleichenberg, Austria, to harness the therapeutic benefits of the farm environment.

Contemporary examples of the farm effect can be observed in traditional farming communities such as the Amish and Old Order Mennonites, who exhibit significantly lower rates of allergic diseases compared to urban populations or traditional farming communities that have adopted a modern lifestyle (Figure 5) [29, 34]. Studies indicate that the protective influence of farm life is especially evident in reducing the prevalence of atopic asthma and atopic dermatitis, whereas urban environments show little to no such benefit.

However, it is now increasingly recognized that both "farm" and "urban" environments are heterogeneous and context dependent. Variability in microbial exposure, hygiene standards, pollutant levels, farming practices, and chemical use can significantly influence immune development and disease outcomes. Not all farms confer the same level of microbial diversity, and

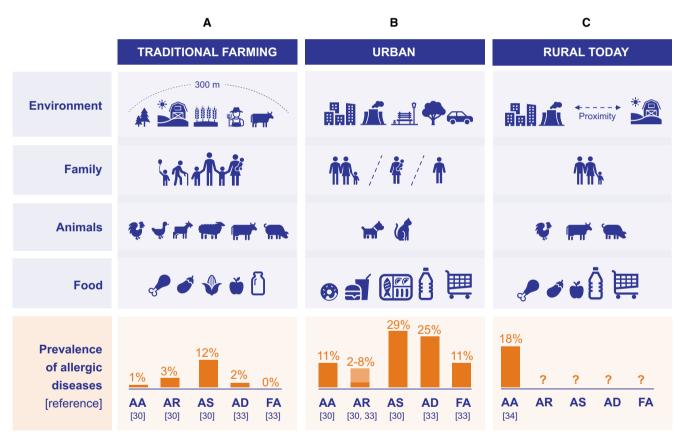


FIGURE 4 | Urbanization: Loss of the farm effect over time. (A) Traditional farming comprises living in a greener environment, with less pollution, and contact to husbandry, especially cattle, in a diameter of 300 m. Typically farm families comprise more children and several generations of the family living together, and close to many different animals. There is healthy stimulation of the immune system by dirt, proteins excreted from cattle such as beta-lactoglobulin (BLG) and exposure to a diversity of microbiota. The farm factor comprises aerosolized compounds from the stables as well as drinking unpasteurized cow's milk. In this setting, the prevalence's of allergic Asthma (AA), allergic Rhinitis (AR), atopic sensitization (AS), atopic dermatitis (AD) and food allergy (FA) is low [28, 29]. (B) In the urban environment the pollution is higher and proximity to traffic much closer, typically families have less children, instead pet cats or dogs are parented in apartments. Urban people have access only to pasteurized dairy products and other processed food in supermarkets. There is generally fewer green spaces, more environmentally stressed plants with higher allergen production, and higher hygiene conditions than on a farm. The prevalence of atopic and allergic diseases reaches considerable numbers [28, 29]. (C) As cities expand and grow together, cities and their suburbs merge with villages. In addition, highways are built close to smaller villages, transporting processed food and pasteurized milk back to the rural population, in fact to the place where the raw food comes from. Hence, the previously rural population today shops in supermarkets and takes also larger distances with cars on a daily base. Thereby, plants also in rural areas are damaged by pollution, and studies point indicate that the farm effect is continuously lost [30]. This is why we need alternatives to supply people with the farm effect.

#### **AMISH COMMUNITIES**



- Rejection of modern technology (e.g. no smartphones, cars, TVs)
- Reliance on self-sustained organic farming with no pesticides
- Absence of processed foods and commercial household products
- Minimal exposure to industrial pollutants and high hygiene environments

#### MENNONITES AND HUTTERITES COMMUNITIES

- Adoption of modern technology, including cars and communal vehicles
- Use of industrial farming methods and communal food production
- Higher consumption of processed foods and use of commercial hygiene products
- Increased urbanization and exposure to high-hygiene environments



FIGURE 5 | Contrasting lifestyles and environmental exposures: The Amish vs. Mennonite/Hutterite Communities and Implications for AD and Allergic Disease Risk. Amish communities follow a conservative, technology-averse lifestyle with homegrown food, minimal processed products, and limited exposure to synthetic chemicals and pollutants. In contrast, Hutterite and many Mennonite groups have adopted more progressive practices, including industrialized farming, communal vehicles, processed foods, and modern hygiene practices. These lifestyle contrasts may contribute to observed differences in immune system development and prevalence of allergic diseases, supporting the role of environmental and exposomic factors in allergy pathogenesis.

urban areas differ widely in lifestyle and environmental quality. These differences are critical to interpreting studies on environmental contributions to allergy risk.

Additionally, the protective benefits of traditional farming environments are diminishing due to climate change, urban sprawl, and changes in agricultural practices. Modern farms have become more industrialized and hygienic, reducing environmental microbial exposure. For instance, while asthma prevalence in children raised on farms was once extremely low (0.8% in previous generations), recent data show an increase to 18% [30]. This decline in the farm effect underscores the urgent need for biomarkers and models that can accurately compare the immunological impacts of different lifestyles [29] (Figures 4 and 5).

Cow's milk, particularly in its raw form, is a nutritionally rich food that has demonstrated strong protective effects against asthma, hay fever, atopic sensitization, and atopic dermatitis [35]. The protective components of raw milk include immuno-modulatory factors such as soluble cytokines, TGF- $\beta$ , immunoglobulins, and bacterial-derived compounds [30]. One notable component is beta-lactoglobulin (BLG), a member of the lipocalin family with key immunological functions in allergy modulation [36]. BLG is also aerosolized in farm dust due to its presence in cow urine, contributing to airborne immune exposures [37].

Despite its benefits, raw milk consumption poses risks due to potential contamination with harmful pathogens and is therefore not recommended for general use. Nevertheless, raw milk provides immunonutrients that help regulate immune responses, whereas pasteurized milk may lack these protective factors and can even contribute to inflammation [38]. Processing methods—such as ultrafiltration, acidification, pasteurization, and homogenization—can alter milk's structure, reduce micronutrient content, and increase allergenicity [39]. These structural

changes, including protein denaturation and separation, diminish milk's immunological benefits.

As a result, current research is focused on developing minimally processed milk alternatives that retain safety while preserving immunological advantages. Strategies under investigation include replicating beneficial raw milk components, such as BLG, in nutritional rather than aerosolized formats, making them more practical and safer for clinical application [40, 41]. In sum, rapid changes in both environmental conditions and food processing practices are shifting immune responses toward a more proinflammatory profile, potentially contributing to the rising burden of atopic diseases.

# **5** | Planetary Health, Climate Change, and Atopic Dermatitis

Climate change profoundly impacts human health, affecting nearly every system in the body—from the skin to the brain, cardiovascular system, and beyond. This connection is evident in the interplay between tipping points in the Earth's systems and human health, particularly the immune system. Disruptions in immune balance can trigger allergic diseases, while tipping points in Earth's ecosystems can destabilize the climate. If current trends persist, humanity risks losing its climate niche, with an estimated three billion people potentially displaced in the next 50 years due to climate-related events [42]. The World Economic Forum has highlighted the importance of addressing climate change, which is impacting human health, including skin, with extreme weather events, heat, and pollen having a significant impact [43]. The analysis revealed that by 2050, climate change could result in an additional 14.5 million deaths and \$12.5 trillion in global economic losses. Furthermore, climate-related impacts are projected to add \$1.1 trillion in healthcare costs, placing substantial pressure on already overburdened healthcare

systems, infrastructures, and medical resources worldwide [43]. Over the next decade, as detailed in the World Economic Forum Risks Report 2023, the failure to mitigate and adapt to climate change will represent our gravest risk globally [43].

The skin barrier plays a central role in understanding how climate change and environmental factors affect atopic dermatitis (AD) [44]. This barrier is a complex system orchestrated by multiple components, including the microbiome, chemical barrier, physical barrier, immune barrier, and the neurological barrier [45]. Pollution poses a dual threat as it directly harms human health while accelerating climate change and biodiversity loss. It significantly impacts the skin barrier, with evidence showing traffic pollution as a risk factor for AD, where children living near high-traffic areas are at a higher risk of developing the condition. Pollutants such as PM10 and black carbon damage the skin and mucosal barriers, with molecular evidence linking them to inflammation and dysfunction [46]. On the other hand, air pollution and climate change have a significant impact on pollen, a trigger for a subgroup of patients with AD. Pollens under the influence of pollution are becoming more aggressive by increasing their production of allergens and/or proinflammatory mediators from pollen. Extreme weather events also contribute to this effect by inducing thunderstorm asthma [47]. Concerning the impact of climate change on ecosystems, one can conclude that there are four main effects on pollen: a longer pollen season, more pollen per day, more aggressive pollen that produces more allergens, and the introduction of new pollen types, such as ambrosia [48]. Recent data indicate that elevated CO2 levels lead to pollen with an enhanced capacity to trigger loss of immune tolerance and increased lung inflammation in a mouse model [49]. Notably, beyond being allergen carriers and allergy inducers, pollens induce symptoms also in non-allergics and can block antiviral genes in the noses of both allergics and non-allergics [50]. Pollen blocks type I and type III interferon on the mucosa of patients and healthy individuals, leading to a block of antiviral activity, which may have contributed to the exponential increase in COVID-19 infections during the pandemic [51].

The skin barrier, air pollution, and pollen serve as critical intersections between climate change and human health. By understanding these mechanisms, we can better address the rising burden of atopic dermatitis and related conditions in a changing environment. These findings underscore the urgent need for policies targeting pollution reduction, biodiversity conservation, and climate protection to safeguard human health.

### 6 | Prevention by Vaccination Against the Mounting Challenge of Allergic Disorders: The Example of Veterinary Medicine

Vaccination practices in animals, particularly pets and livestock, are an integral aspect of the One Health framework targeting animal vectors of infectious diseases [52]. In the context of AD, vaccination may indirectly influence disease dynamics by shaping the immune profiles of companion animals and modifying their microbiomes [53], which may in turn affect human inhabitants through microbiota sharing and allergen exposure. In veterinary medicine, the potential adverse effects of frequent revaccination in companion animals on triggering dysimmunity hold potential

relevance to the One Health framework, especially in relation to immune-mediated diseases [54] (Box 2).

Coming across limitations in the availability of allergens or classical desensitization approaches, targeting key molecules linked to the underlying pathological mechanism suggests correction or re-education of the allergic immune responses. In veterinary medicine, monoclonal antibodies against key pathway molecules are registered for use in dogs and cats, but their application is mostly restricted to these species due to market size and possibly body weight considerations [55]. The cost of monoclonal antibody treatment is high, with an annual treatment for a 3-10-kg dog costing around 1000 EUR. This cost increases significantly for larger animals like horses, leading to a preventive approach by vaccination. This strategy uses a vaccine that induces selfmade autoantibodies, which requires a strong immune activator to overcome B cell tolerance [55]. A virus-like particle serves as the immune activator, which is cost-effective and can be produced in a procaryotic expression system [56]. Vaccines are not applied based on body weight, but rather on a threshold activation, making the dose independent of body weight.

To proof the concept of autovaccination in diseased animals, an IL-5 vaccine has been developed for the use in equine allergy characterized by hypereosinophilia. Targeting eosinophils has a broad effect on allergies, affecting eosinophils, basophils, allergen-specific IgE, and thus covering thus the three most important components in allergy. By reducing the level of eosinophils in the blood and skin through interleukin 5 targeting in an allergen-independent manner, treating allergies in animals where the specific allergen is unknown is theoretically possible. The two diseases being targeted by the vaccine are insect bite hypersensitivity and urticaria in horses, both common allergic diseases in horses. The vaccine was able to significantly reduce clinical signs of the skin for both allergies [55, 57]. The safety of vaccinating against a self-protein is a concern, but no safety signals were found in clinical studies, including a fiveyear follow-up with yearly revaccinations [58]. This approach can be extended to molecules more relevant to atopic dermatitis

### $BOX\ 2\ \mid\$ One Health perspective on vaccination and atopic dermatitis.

- Vaccination affects more than disease prevention: Animal vaccination practices can influence microbial exposure in shared environments, shaping the immune systems of both animals and humans.
- Overvaccination and immune modulation: Some speculate that frequent or adjuvanted vaccinations may alter immune balance, though evidence linking this directly to atopic dermatitis (AD) is limited.
- Microbiome and allergen exposure: Vaccinated animals may exhibit altered microbiota or skin barrier functions, potentially affecting human habitants via shared environments.
- Implication: Immune health in animals is intertwined with human health—highlighting the need for coordinated vaccination strategies under the One Health model.

(AD), where—in contrast to asthma—therapeutic strategies targeting eosinophils have not been successful. For instance, interleukin-31 (IL-31), a key mediator in pruritic allergic conditions, has emerged as a leading target in veterinary medicine. A caninized monoclonal antibody, lokivetmab, has been available since 2016 for the treatment of atopic dermatitis and allergic pruritus in dogs [59]. Similar to the IL-5 vaccine strategy, IL-31 vaccination has been evaluated in dogs and horses. In dogs immunized against canine IL-31, a reduction in pruritic symptoms was observed, with efficacy correlating strongly with high antibody titers [60].

### 7 | How Web Data Mining Can Shape Interactome Research in AD

Data mining analyzes various databases and sources, providing a new approach to understanding diseases like AD through the One Health lens. Google search volume data illustrates how people seek information online [61]. A good example is that of a total solar eclipse in April 2024, where people damaged their eyes and then searched for information online. From a medical perspective, analyzing online search data can provide insights into the digital patient journey, which is the path from the first symptoms to diagnosis and treatment. The digital patient journey is highly individualized, influenced by comorbidities, environment, and social context, and can be analyzed using online search data and social media. In Europe, over 90% of the population uses the internet to look up health information, and analyzing this data can provide valuable insights into disease patterns and trends. Hay fever searches illustrate how online search data can reflect seasonal patterns and geographic variations in disease interest [62]. Comparing web search interest between countries can also provide insights into disease patterns, as seen in the example of hay fever searches in Sweden and Germany. Analyzing online search data can help identify unmet needs, raise awareness, and provide insights into disease patterns. AD shows a clear seasonal interest from the general population. Every year, it peaks in February, March, and May, and then decreases in the summer when it gets warmer [63]. In Germany, over four consecutive years, it was found that half of the population is interested in specific localizations of affected body parts, with a quarter of patients interested in AD affecting the face, eyes, hands, and head [64]. Analyzing online data can help assess influencing factors on an individual level and understand what people are looking up when searching for information related to AD: most individuals searching for information on AD are looking for general information about the disease, while 10% are interested in treatment options, and only a small proportion are interested in modern treatments like biologicals. Home remedies are a major area of interest for people searching for information on AD, highlighting the need to raise awareness about available treatment options and counter misinformation [65-67].

Environmental factors have a clear influence on AD, with seasonal variations in interest in the condition connected to climate, and countries with a continental climate showing higher peaks of interest [66]. In Sweden, higher temperatures and more sun are associated with less interest in AD, while more wind is a trigger factor for the condition [63]. Spatial epidemiology

provides real-time data to identify unmet needs on a population-based level. For AD, a clear seasonal peak in different areas of Europe can be used for disease education, treatment, and raising awareness. Searches on Google can be used to identify correlations between environmental factors and diseases. In Munich, a connection has been found between birch pollen and atopic dermatitis, with a clear correlation between the amount of pollen measured and the interest of the general population in atopic dermatitis [66].

An analogy with the story of John Snow, who in 1854 discovered the connection between cholera deaths and water pumps [68], illustrates the concept of correlation and its significance in understanding diseases. By comparing real data on disease incidence and prevalence with web search data, a clear connection can be seen in countries where both data are available, such as in the case of sarcoidosis in Sweden [69]. Web search data can also be a powerful tool to identify regional levels, unmet needs, and risk factors for diseases, especially in countries where general information on disease incidence and prevalence is not available.

The next step in data mining involves analyzing patterns of data on a personal level, using variables such as smart lenses, smart watches, and smart homes to assess data on heart rate, breathing, and transepidermal water loss. Such data can be used to identify connections between diseases, such as AD, and environmental and climate factors on a personal and individual level [62]. Recently, environmental genomics revealed that Streptococcus strains were dominant in human-derived wastewater, with operational taxonomic units that were strongly associated with inflammation-inducing bacteria originating from AD patients [70].

#### 8 | One Health Lens AD Questioning

### 8.1 | Link Infectious Diseases-Allergic Diseases

The One Health concept of is relevant in the field of complex diseases such as atopic dermatitis, and there is a need for further research on the relationship between infectious diseases and allergies. The hygiene/biodiversity hypothesis suggests that a decrease in exposure to certain microscopic organisms may lead to an increase in allergies, and a recent study found that people who survived the 1346 plague in Europe had changes in gene expression that may have contributed to the development of allergies and autoimmune diseases [71]. Vaccination policies in humans and animals may also influence immune-mediated diseases including AD (Box 2).

#### 8.2 | Foods

The timing and route (skin vs. GI tract) of exposure to allergens play a crucial role in the development of allergies, with early exposure to certain allergens, such as peanuts, potentially leading to tolerance, while exposure through the skin can lead to sensitization [72]. Processing of food, particularly roasting, can increase the allergenic potential of the major allergen ara h1, posing a danger signal to the immune system [73]. Analogously, the highly processed pet food industry has grown significantly

over the past 50 years, with a parallel development of allergies in animals, and it is unclear whether the use of ultra-processed food contributes to this trend. There is limited research on the impact of pet food processing on allergies in animals due to strong lobbying in the industry, but a Swedish study suggested that feeding raw food to dogs may help prevent atopic dermatitis [74]. However, this study is limited by multiple possible biases: owners of cases or owners feeding home-cooked foods could be more motivated than controls [75]. On the other hand, a study found that dogs with more allergies were eating more raw food diets, but this could be due to owners changing their dogs' diets after symptoms appeared, as suggested by veterinarians [76]. Immunonutrients, such as vitamin A and folic acid, play a crucial role in preventing atopic dermatitis, but efficiently delivering these nutrients to the body can be challenging due to the hepcidin block that blocks iron absorption in atopic patients [77]. Functional iron deficiency may result [78] and has also been observed in CAD [79]. Iron has a special importance in preventing allergic symptoms, as it helps calm down immune cells, particularly regulatory T cells, which secure intracellular iron levels by expressing ferritin heavy chain (FTH) and transferrin receptor [80]. Targeted nutrition approaches are necessary to bring substances to immune cells, making a difference between commercial supplements and specific dietary approaches.

#### 8.3 | Cleansing Agents and Detergents

Cleaning agents—particularly harsh or antimicrobial products—can significantly disrupt the skin barrier and microbiome, playing a contributory role in the pathogenesis and exacerbation of AD. Many conventional cleaning products contain surfactants, preservatives, and solvents (e.g., quaternary ammonium compounds, bleach, or agents) that strip lipids from the skin, increase transepidermal water loss, and impair the epidermal barrier. This barrier disruption not only makes the skin more susceptible to allergens and irritants but also promotes inflammation and dysbiosis—an imbalance in the skin's microbial communities that is characteristic of AD [81]. From a One Health perspective, the widespread use of biocidal cleaning agents also impacts indoor environmental microbiota and the microbial exposures shared by humans and animals. Over-sanitized home environments reduce microbial diversity, which may impair immune tolerance, especially in early life. Additionally, pets exposed to the same household cleaning routines can experience skin barrier alterations and shifts in their own microbiomes, creating a shared ecological imbalance that may influence human health via the skin or respiratory tract.

## 8.4 | Interaction Between Pollens and Airborne Pollutants

Children exposed to pollen early in life have a higher probability of developing asthma and sensitization, highlighting the importance of considering both timing and route of exposure [82]. Research has shown differences in the prevalence of asthma in rural and urban China, with many Chinese studies currently exploring this topic [83]. So, monitoring and targeting preventive airborne interventions at the individual and population levels is important.

# 8.5 | Climate Change's Effects on Insect-Plant Interaction and Disease Vectors

Although direct consequences for AD itself are currently speculative, climate change is significantly altering insectplant interactions, which have implications for allergy prevalence and severity. Rising temperatures and elevated CO<sub>2</sub> levels are disrupting the synchrony between plants and their insect pollinators. For instance, warming accelerates plant phenology, leading to mismatches between flowering times and insect activity, which can affect pollination success and plant reproductive output. Additionally, climate-induced shifts in insect populations can influence the distribution and abundance of allergenic plants. Changes in herbivore pressure may alter plant community composition, potentially increasing the prevalence of species that produce allergenic pollen [84]. In addition, climate change is driving significant ecological and climatic shifts that influence disease vectors. These changes are reshaping both infectious disease dynamics and allergic disease prevalence in multiple ways. The spread of ticks, facilitated by climate change, has been linked to the emergence of alphagal syndrome—red meat allergy caused by the sugar molecule transmitted during bites. Changes in precipitation and humidity affect the reproduction and survival of both vectors and allergenic plants/molds. Disruption of ecosystems alters habitats and predator-prey relationships, which may increase vector populations or shift plant species dominance toward more allergenic varieties (e.g., ragweed) [85].

#### 8.6 | Pet and Domestic Animals

Pets, especially cats and dogs, share living spaces with humans and are exposed to household cleaners, personal care products, air pollutants, and microplastics. The utilization of cosmetic products and food additives for pets is on the rise, unfortunately, accompanied by less rigorous safety regulations than those governing human products [86]. In rural China, people often live with chickens in their homes, which may provide similar protective factors against allergies as living with cows or pigs in European rural areas [87]. Cat allergy is common in humans with or without AD and is usually caused by the major cat allergen Fel d 1. Currently, there is no efficient and safe therapy for cat allergy available. A new strategy to treat Fel d 1-induced allergy in human subjects by immunizing cats against their own major allergen, Fel d 1is in an advanced development phase [88].

#### 8.7 | What Is a "Healthy Planet"?

The concept of a "healthy planet" is defined from an anthropocentric view, meaning a planet that is healthy for humans, but not necessarily for the planet itself, as it has undergone changes throughout its history. The definition of a healthy planet is subjective and can be influenced by human perspectives, with the primary goal being to save the planet for human survival, rather than the planet's own well-being. The health of the planet is not just limited to humans and animals, but also includes plants, which are also suffering from diseases and environmental changes. Climate change may increase plant viral load in pollen, lengthen the transmission window, expand the geographical and

host range of pollen-associated viruses, enhance pollen-based dispersal through changes in plant phenology and pollinator activity [72]. Trees are already dying due to environmental sensitivity, with some species, such as birch trees, potentially disappearing in the next 50 years [89]. Plant diseases, such as those caused by osmotic stress and dryness, can lead to an increase in allergens, and high  ${\rm CO_2}$  levels can affect plant growth and iron absorption, making them more allergenic [90]. The relationship between plant diseases and allergens is complex, and further research is needed to understand the implications of climate change on plant health and human allergies [91].

#### 9 | Conclusions and Future Directions

- The objective of the workshop was to pave the way for further work and collaboration with different specialties, such as human and veterinary medicine, epidemiology, and others.
- The One Health concept is relevant to atopic dermatitis, and the symposium showed that a One Health approach is already being taken to solve complex issues.
- The evidence suggests that allergies and atopic dermatitis are environmentally triggered, with urbanization and pollution being a significant trigger, which supports their classification as non-communicable diseases by the World Health Organization (WHO).
- The planetary Health discussion brings things into context in a broad way, and it is essential to connect the dots and use evidence and data to help countries make policies.
- The impacts of climate change and biodiversity loss on ecosystems are enormous, and reducing emissions and overuse of natural capital should be the top priority to mitigate its effects.

#### **Author Contributions**

Conceptualization: A.T. (choice of topic) and all authors for respective/dedicated sections. Preparation, creation, and/or presentation of the published work, specifically visualization/data presentation: A.T., P.P., and all authors. Writing – original draft: A.T. Writing – review and editing: all authors.

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#### **Ethics Statement**

The authors have nothing to report.

#### **Conflicts of Interest**

A.F.-G. is a shareholder of Biomedical Int. R+D GmbH, Vienna, Austria. A.G. is involved in the development of therapeutic equine vaccines. The other authors declare no conflicts of interest.

#### **Data Availability Statement**

The authors have nothing to report.

#### References

- 1. One Health High-Level Expert Panel (OHHLEP), W. B. Adisasmito, S. Almuhairi, et al., "One Health: A New Definition for a Sustainable and Healthy Future," *PLoS Pathogens* 18, no. 23 (2022): e1010537, https://doi.org/10.1371/journal.ppat.1010537.
- 2. H. L. Brown, I. G. Pursley, D. L. Horton, and R. M. La Ragione, "One Health: A Structured Review and Commentary on Trends and Themes," *One Health Outlook* 6, no. 1 (2024): 17, https://doi.org/10.1186/s42522-024-00111-x.
- 3. FAO, UNEP, WHO, and WOAH, "One Health Joint Plan of Action (2022–2026)," Working Together for the Health of Humans, Animals, Plants, and the Environment, Rome (2022), https://doi.org/10.4060/cc2289en.
- 4. G. Laing, M. A. N. Vigilato, S. Cleaveland, et al., "One Health for Neglected Tropical Diseases," *Transactions of the Royal Society of Tropical Medicine and Hygiene* 115, no. 2 (2021): 182–184, https://doi.org/10.1093/trstmh/traa117. Erratum in: *Transactions of the Royal Society of Tropical Medicine and Hygiene* 115, no. 8 (2021): 940, https://doi.org/10.1093/trstmh/trab086.
- 5. R. R. Yotsu, L. C. Fuller, M. E. Murdoch, et al., "A Global Call for Action to Tackle Skin-Related Neglected Tropical Diseases (Skin NTDs) Through Integration: An Ambitious Step Change," *PLoS Neglected Tropical Diseases* 17, no. 6 (2023): e0011357, https://doi.org/10.1371/journal.pntd.0011357.
- 6. P. Schmid-Grendelmeier, F. Rapelanoro Rabenja, A. M. Beshah, et al., "How to Integrate Atopic Dermatitis in the Management of Skin Neglected Tropical Diseases in Sub-Saharan Africa?," *Journal of the European Academy of Dermatology and Venereology* 37 (2023): e1040–e1042, https://doi.org/10.1111/jdv.19096.
- 7. H. Renz, P. G. Holt, M. Inouye, A. C. Logan, S. L. Prescott, and P. D. Sly, "An Exposome Perspective: Early-Life Events and Immune Development in a Changing World," *Journal of Allergy and Clinical Immunology* 140, no. 1 (2017): 24–40, https://doi.org/10.1016/j.jaci. 2017.05.015.
- 8. C. A. Akdis, "Does the Epithelial Barrier Hypothesis Explain the Increase in Allergy, Autoimmunity and Other Chronic Conditions?," *Nature Reviews. Immunology* 21, no. 11 (2021): 739–751, https://doi.org/10.1038/s41577-021-00538-7.
- 9. Z. Celebi Sozener, B. Ozdel Ozturk, P. Cerci, et al., "Epithelial Barrier Hypothesis: Effect of the External Exposome on the Microbiome and Epithelial Barriers in Allergic Disease," *Allergy* 77, no. 5 (2022): 1418–1449, https://doi.org/10.1111/all.15240.
- 10. A. D. Irvine, W. H. McLean, and D. Y. Leung, "Filaggrin Mutations Associated With Skin and Allergic Diseases," *New England Journal of Medicine* 365, no. 14 (2011): 1315–1327, https://doi.org/10.1056/NEJMra1011040.
- 11. C. Traidl-Hoffmann, J. Afghani, C. A. Akdis, et al., "Navigating the Evolving Landscape of Atopic Dermatitis: Challenges and Future Opportunities: The 4th Davos Declaration," *Allergy* 79, no. 10 (2024): 2605–2624, https://doi.org/10.1111/all.16247.
- 12. D. P. Strachan, "Family Size, Infection and Atopy: The First Decade of the 'Hygiene Hypothesis'," *Thorax* 55, no. Suppl 1 (2000): S2–S10, https://doi.org/10.1136/thorax.55.suppl\_1.s2.
- 13. L. von Hertzen, I. Hanski, and T. Haahtela, "Natural Immunity. Biodiversity Loss and Inflammatory Diseases Are Two Global Megatrends That Might Be Related," *EMBO Reports* 12, no. 11 (2011): 1089–1093, https://doi.org/10.1038/embor.2011.195.
- 14. K. Donald and B. B. Finlay, "Early Life Interactions Between the Microbiota and Immune System: Impact on Immune System Development and Atopic Disease," *Nature Reviews Immunology* 23, no. 11 (2023): 735–748, https://doi.org/10.1038/s41577-023-00874-w.
- 15. J. Orasche, K. C. Nadeau, A. Schuster, J. Rockström, C. A. Akdis, and C. Traidl-Hoffmann, "Climate Crisis Paralysis: Accelerating Global

- Action for Health Resilience in a Changing World," *Allergy* 79, no. 7 (2024): 1653–1655, https://doi.org/10.1111/all.16096.
- 16. C. Traidl-Hoffmann, S. M. John, and A. Zink, "Klimawandel Geht Unter Die Haut [Climate Change Gets Under the Skin]," *Dermatologie (Heidelberg)* 75, no. 2 (2024): 91–92, https://doi.org/10.1007/s00105-023-05290-8.
- 17. W. Lee, F. Chaudhary, and D. K. Agrawal, "Environmental Influences on Atopic Eczema," *Journal of Environmental Science and Public Health* 8, no. 2 (2024): 101–115, https://doi.org/10.26502/jesph.96120209.
- 18. S. P. Wang, N. Stefanovic, R. L. Orfali, et al., "Impact of Climate Change on Atopic Dermatitis: A Review by the International Eczema Council," *Allergy* 79, no. 6 (2024): 1455–1469, https://doi.org/10.1111/all.16007.
- 19. C. Indolfi, E. D'Addio, C. L. Bencivenga, et al., "The Primary Prevention of Atopy: Does Early Exposure to Cats and Dogs Prevent the Development of Allergy and Asthma in Children? A Comprehensive Analysis of the Literature," *Life (Basel)* 13, no. 9 (2023): 1859, https://doi.org/10.3390/life13091859.
- 20. S. K. Park, J. S. Kim, and H. M. Seo, "Exposure to Air Pollution and Incidence of Atopic Dermatitis in the General Population: A National Population-Based Retrospective Cohort Study," *Journal of the American Academy of Dermatology* 87, no. 6 (2022): 1321–1327, https://doi.org/10.1016/j.jaad.2021.05.061.
- 21. R. Halliwell, C. M. Pucheu-Haston, T. Olivry, et al., "Feline Allergic Diseases: Introduction and Proposed Nomenclature," *Veterinary Dermatology* 32, no. 1 (2021): 8-e2, https://doi.org/10.1111/vde.12899.
- 22. S. Wilhem, M. Kovalik, and C. Favrot, "Breed-Associated Phenotypes in Canine Atopic Dermatitis," *Veterinary Dermatology* 22, no. 2 (2011): 143–149, https://doi.org/10.1111/j.1365-3164.2010.00925.x.
- 23. J. Lehtimäki, H. Sinkko, A. Hielm-Björkman, et al., "Skin Microbiota and Allergic Symptoms Associate With Exposure to Environmental Microbes," *Proceedings of the National Academy of Sciences of the United States of America* 115, no. 19 (2018): 4897–4902, https://doi.org/10.1073/pnas.1719785115.
- 24. J. Lehtimäki, H. Sinkko, A. Hielm-Björkman, T. Laatikainen, L. Ruokolainen, and H. Lohi, "Simultaneous Allergic Traits in Dogs and Their Owners Are Associated With Living Environment, Lifestyle and Microbial Exposures," *Scientific Reports* 10, no. 1 (2020): 21954, https://doi.org/10.1038/s41598-020-79055-x.
- 25. E. Hakanen, J. Lehtimäki, E. Salmela, et al., "Urban Environment Predisposes Dogs and Their Owners to Allergic Symptoms," *Scientific Reports* 8, no. 1 (2018): 1585, https://doi.org/10.1038/s41598-018-19953-3.
- 26. Z. Parr-Cortes, C. T. Müller, L. Talas, M. Mendl, C. Guest, and N. J. Rooney, "The Odour of an Unfamiliar Stressed or Relaxed Person Affects Dogs' Responses to a Cognitive Bias Test," *Scientific Reports* 14, no. 1 (2024): 15843, https://doi.org/10.1038/s41598-024-66147-1.
- 27. J. Puurunen, E. Hakanen, M. K. Salonen, et al., "Inadequate Socialisation, Inactivity, and Urban Living Environment Are Associated With Social Fearfulness in Pet Dogs," *Scientific Reports* 10, no. 1 (2020): 3527, https://doi.org/10.1038/s41598-020-60546-w.
- 28. J. Riedler, C. Braun-Fahrländer, W. Eder, et al., "Exposure to Farming in Early Life and Development of Asthma and Allergy: A Cross-Sectional Survey," *Lancet* 358, no. 9288 (2001): 1129–1133, https://doi.org/10.1016/S0140-6736(01)06252-3.
- 29. K. M. Järvinen, E. C. Davis, E. Bevec, et al., "Biomarkers of Development of Immunity and Allergic Diseases in Farming and Non-Farming Lifestyle Infants: Design, Methods and 1 Year Outcomes in the 'Zooming in to Old Order Mennonites' Birth Cohort Study," *Frontiers in Pediatrics* 10 (2022): 916184, https://doi.org/10.3389/fped. 2022.916184.
- 30. M. K. Madsen, V. Schlünssen, C. Svanes, et al., "The Effect of Farming Environment on Asthma; Time Dependent or Universal?,"

- *European Journal of Epidemiology* 37, no. 8 (2022): 779–788, https://doi.org/10.1007/s10654-022-00893-2.
- 31. T. Brick, K. Hettinga, B. Kirchner, M. W. Pfaffl, and M. J. Ege, "The Beneficial Effect of Farm Milk Consumption on Asthma, Allergies, and Infections: From Meta-Analysis of Evidence to Clinical Trial," *Journal of Allergy and Clinical Immunology. In Practice* 8, no. 3 (2020): 878–889. e3, https://doi.org/10.1016/j.jaip.2019.11.017.
- 32. G. Loss, S. Apprich, M. Waser, et al., "The Protective Effect of Farm Milk Consumption on Childhood Asthma and Atopy: The GABRIELA Study," *Journal of Allergy and Clinical Immunology* 128, no. 4 (2011): 766–773.e4, https://doi.org/10.1016/j.jaci.2011.07.048.
- 33. C. A. Steiman, M. D. Evans, K. E. Lee, et al., "Patterns of Farm Exposure Are Associated With Reduced Incidence of Atopic Dermatitis in Early Life," *Journal of Allergy and Clinical Immunology* 146, no. 6 (2020): 1379–1386.e6, https://doi.org/10.1016/j.jaci.2020.06.025.
- 34. C. Ober, A. I. Sperling, E. von Mutius, and D. Vercelli, "Immune Development and Environment: Lessons From Amish and Hutterite Children," *Current Opinion in Immunology* 48 (2017): 51–60, https://doi.org/10.1016/j.coi.2017.08.003.
- 35. S. Abbring, G. Hols, J. Garssen, and B. C. A. M. van Esch, "Raw Cow's Milk Consumption and Allergic Diseases—The Potential Role of Bioactive Whey Proteins," *European Journal of Pharmacology* 843 (2019): 55–65, https://doi.org/10.1016/j.ejphar.2018.11.013.
- 36. S. M. Afify, I. Pali-Schöll, K. Hufnagl, et al., "Bovine Holo-Beta-Lactoglobulin Cross-Protects Against Pollen Allergies in an Innate Manner in BALB/c Mice: Potential Model for the Farm Effect," *Frontiers in Immunology* 12 (2021): 611474, https://doi.org/10.3389/fimmu. 2021.611474.
- 37. I. Pali-Schöll, R. Bianchini, S. M. Afify, et al., "Secretory Protein Beta-Lactoglobulin in Cattle Stable Dust May Contribute to the Allergy-Protective Farm Effect," *Clinical and Translational Allergy* 12, no. 2 (2022): e12125, https://doi.org/10.1002/clt2.12125.
- 38. F. Roth-Walter, S. M. Afify, L. F. Pacios, et al., "Cow's Milk Protein  $\beta$ -Lactoglobulin Confers Resilience Against Allergy by Targeting Complexed Iron Into Immune Cells," *Journal of Allergy and Clinical Immunology* 147, no. 1 (2021): 321–334.e4, https://doi.org/10.1016/j.jaci.2020.05.023.
- 39. S. A. Jensen, A. Fiocchi, T. Baars, et al., "Diagnosis and Rationale for Action Against Cow's Milk Allergy (DRACMA) Guidelines Update-III—Cow's Milk Allergens and Mechanisms Triggering Immune Activation," *World Allergy Organization Journal* 15, no. 9 (2022): 100668, https://doi.org/10.1016/j.waojou.2022.100668.
- 40. S. Abbring, L. Xiong, M. A. P. Diks, et al., "Loss of Allergy-Protective Capacity of Raw Cow's Milk After Heat Treatment Coincides With Loss of Immunologically Active Whey Proteins," *Food & Function* 11, no. 6 (2020): 4982–4993, https://doi.org/10.1039/d0fo01175d.
- 41. T. Bartosik, S. A. Jensen, S. M. Afify, et al., "Ameliorating Atopy by Compensating Micronutritional Deficiencies in Immune Cells: A Double-Blind Placebo-Controlled Pilot Study," *Journal of Allergy and Clinical Immunology. In Practice* 10, no. 7 (2022): 1889–1902.e9, https://doi.org/10.1016/j.jaip.2022.02.028.
- 42. C. Xu, T. A. Kohler, T. M. Lenton, J. C. Svenning, and M. Scheffer, "Future of the Human Climate Niche," *Proceedings of the National Academy of Sciences of the United States of America* 117, no. 21 (2020): 11350–11355, https://doi.org/10.1073/pnas.1910114117.
- 43. "Quantifying the Impact of Climate Change on Human Health," accessed May 15, 2025, https://www.weforum.org/publications/quant ifying-the-impact-of-climate-change-on-human-health/.
- 44. T. Luger, M. Amagai, B. Dreno, et al., "Atopic Dermatitis: Role of the Skin Barrier, Environment, Microbiome, and Therapeutic Agents," *Journal of Dermatological Science* 102, no. 3 (2021): 142–157, https://doi.org/10.1016/j.jdermsci.2021.04.007.

- 45. S. Eyerich, K. Eyerich, C. Traidl-Hoffmann, and T. Biedermann, "Cutaneous Barriers and Skin Immunity: Differentiating A Connected Network," *Trends in Immunology* 39, no. 4 (2018): 315–327, https://doi.org/10.1016/j.it.2018.02.004.
- 46. U. Krämer, D. Sugiri, U. Ranft, et al., "Eczema, Respiratory Allergies, and Traffic-Related Air Pollution in Birth cOne Healthorts From Small-Town Areas," *Journal of Dermatological Science* 56, no. 2 (2009): 99–105, https://doi.org/10.1016/j.jdermsci.2009.07.014.
- 47. A. Straub, V. Fricke, P. Olschewski, et al., "The Phenomenon of Thunderstorm Asthma in Bavaria, Southern Germany: A Statistical Approach," *International Journal of Environmental Health Research* 32, no. 12 (2022): 2678–2694, https://doi.org/10.1080/09603123.2021. 1985971.
- 48. J. Rojo, J. Oteros, A. Picornell, et al., "Effects of Future Climate Change on Birch Abundance and Their Pollen Load," *Global Change Biology* 27, no. 22 (2021): 5934–5949, https://doi.org/10.1111/gcb.15824.
- 49. D. Rauer, S. Gilles, M. Wimmer, et al., "Ragweed Plants Grown Under Elevated  ${\rm CO_2}$  Levels Produce Pollen Which Elicit Stronger Allergic Lung Inflammation," *Allergy* 76, no. 6 (2021): 1718–1730, https://doi.org/10.1111/all.14618.
- 50. S. Gilles, C. Blume, M. Wimmer, et al., "Pollen Exposure Weakens Innate Defense Against Respiratory Viruses," *Allergy* 75, no. 3 (2020): 576–587, https://doi.org/10.1111/all.14047.
- 51. A. Damialis, S. Gilles, M. Sofiev, et al., "Higher Airborne Pollen Concentrations Correlated With Increased SARS-CoV-2 Infection Rates, as Evidenced From 31 Countries Across the Globe," *Proceedings of the National Academy of Sciences of the United States of America* 118, no. 12 (2021): e2019034118, https://doi.org/10.1073/pnas.2019034118.
- 52. J. Zinsstag, E. Schelling, F. Roth, B. Bonfoh, D. de Savigny, and M. Tanner, "Human Benefits of Animal Interventions for Zoonosis Control," *Emerging Infectious Diseases* 13, no. 4 (2007): 527–531, https://doi.org/10.3201/eid1304.060381.
- 53. D. J. Lynn, S. C. Benson, M. A. Lynn, and B. Pulendran, "Modulation of Immune Responses to Vaccination by the Microbiota: Implications and Potential Mechanisms," *Nature Reviews. Immunology* 22, no. 1 (2022): 33–46, https://doi.org/10.1038/s41577-021-00554-7.
- 54. W. J. Dodds, "More Bumps on the Vaccine Road," *Advances in Veterinary Medicine* 41 (1999): 715–732, https://doi.org/10.1016/s0065-3519(99)80055-x.
- 55. A. Fettelschoss-Gabriel, V. Fettelschoss, F. Thoms, et al., "Treating Insect-Bite Hypersensitivity in Horses With Active Vaccination Against IL-5," *Journal of Allergy and Clinical Immunology* 142, no. 4 (2018): 1194–1205.e3, https://doi.org/10.1016/j.jaci.2018.01.041.
- 56. M. F. Bachmann and M. R. Dyer, "Therapeutic Vaccination for Chronic Diseases: A New Class of Drugs in Sight," *Nature Reviews. Drug Discovery* 3, no. 1 (2004): 81–88, https://doi.org/10.1038/nrd1284.
- 57. K. Birkmann, F. Jebbawi, N. Waldern, et al., "Eosinophils Play a Surprising Leading Role in Recurrent Urticaria in Horses," *Vaccines (Basel)* 12, no. 6 (2024): 562, https://doi.org/10.3390/vaccines12060562.
- 58. S. Jonsdottir, V. Fettelschoss, F. Olomski, et al., "Safety Profile of a Virus-Like Particle-Based Vaccine Targeting Self-Protein Interleukin-5 in Horses," *Vaccine* 8, no. 2 (2020): 213, https://doi.org/10.3390/vaccines8020213.
- 59. M. Gober, A. Hillier, M. A. Vasquez-Hidalgo, D. Amodie, and M. A. Mellencamp, "Use of Cytopoint in the Allergic Dog," *Frontiers in Veterinary Science* 9 (2022): 909776, https://doi.org/10.3389/fvets.2022. 909776.
- 60. M. F. Bachmann, A. Zeltins, G. Kalnins, et al., "Vaccination Against IL-31 for the Treatment of Atopic Dermatitis in Dogs," *Journal of Allergy and Clinical Immunology* 142, no. 1 (2018): 279–281.e1, https://doi.org/10.1016/j.jaci.2017.12.994.

- 61. S. Sitaru, L. Tizek, J. Buters, A. Ekebom, J. E. Wallin, and A. Zink, "Assessing the National Burden of Allergic Asthma by Web-Search Data, Pollen Counts, and Drug Prescriptions in Germany and Sweden," World Allergy Organization Journal 16, no. 2 (2023): 100752, https://doi.org/10.1016/j.waojou.2023.100752.
- 62. A. Schober, L. Tizek, E. K. Johansson, et al., "Monitoring Disease Activity of Pollen Allergies: What Crowdsourced Data Are Telling Us," *World Allergy Organization Journal* 15, no. 12 (2022): 100718, https://doi.org/10.1016/j.waojou.2022.100718.
- 63. L. Tizek, H. Wecker, S. Schneider, E. K. Johansson, Y. Girmay, and A. Zink, "Eczema-Related Web Search Data in Sweden: Investigating Search Patterns and the Influence of Weather," *Acta Dermato-Venereologica* 102 (2022): adv00810, https://doi.org/10.2340/actadv. v102.2937.
- 64. L. Tizek, M. C. Schielein, L. Tizek, and A. Zink, "Atopische Dermatitis—Identifikation von Bedürfnissen der deutschen Bevölkerung mittels Internetsuchanfragen [Atopic Dermatitis-Identifying Needs in the German Population by Internet Search Queries]," *Der Hautarzt* 73, no. 6 (2022): 475–484, https://doi.org/10.1007/s00105-022-04974-x.
- 65. F. Wallnöfer, S. Ziehfreund, H. Wecker, et al., "Disease-Related Internet Use and Its Relevance to the Patient-Physician Relationship in Atopic Dermatitis: A Cross-Sectional Study in Germany," *Dermatitis* 35, no. 5 (2024): 498–507, https://doi.org/10.1089/derm.2023.0368.
- 66. H. Wecker, S. Ziehfreund, S. Sitaru, et al., "Burden of Atopic Dermatitis in Europe: A Population-Centred Approach Leveraging Web Search Data in 21 European Countries," *Journal of the European Academy of Dermatology and Venereology* 38, no. 8 (2024): 1637–1648, https://doi.org/10.1111/jdv.19989.
- 67. L. Tizek, L. Tizek, S. Schneider, et al., "Navigating Through the Healthcare System With Atopic Dermatitis: Analysing Patient Journeys in Germany," *Journal of the European Academy of Dermatology and Venereology* 39, no. 2 (2025): 322–330, https://doi.org/10.1111/jdv.20268.
- 68. S. W. Newsom, "Pioneers in Infection Control: JOne Healthn Snow, Henry Whitehead, the Broad Street Pump, and the Beginnings of Geographical Epidemiology," *Journal of Hospital Infection* 64, no. 3 (2006): 210–216, https://doi.org/10.1016/j.jhin.2006.05.020.
- 69. S. Ziehfreund, L. Tizek, E. V. Arkema, and A. Zink, "Identifying Sarcoidosis Trends Using Web Search and Real-World Data in Sweden: A Retrospective Longitudinal Study," *Scientific Reports* 14, no. 1 (2024): 19260, https://doi.org/10.1038/s41598-024-69223-8.
- 70. S. Oh, H. Byeon, and J. Wijaya, "Digital Health Framework for the Predictive Surveillance and Diagnosis of Atopic Dermatitis," *Water Research* 284 (2025): 124012, https://doi.org/10.1016/j.watres.2025. 124012.
- 71. J. Klunk, T. P. Vilgalys, C. E. Demeure, et al., "Evolution of Immune Genes Is Associated With the Black Death," *Nature* 611, no. 7935 (2022): 312–319, https://doi.org/10.1038/s41586-022-05349-x.
- 72. G. du Toit, T. Tsakok, S. Lack, and G. Lack, "Prevention of Food Allergy," *Journal of Allergy and Clinical Immunology* 137, no. 4 (2016): 998–1010, https://doi.org/10.1016/j.jaci.2016.02.005.
- 73. S. J. Maleki, S. Y. Chung, E. T. Champagne, and J. P. Raufman, "The Effects of Roasting on the Allergenic Properties of Peanut Proteins," *Journal of Allergy and Clinical Immunology* 106, no. 4 (2000): 763–768, https://doi.org/10.1067/mai.2000.109620.
- 74. A. Nødtvedt, K. Bergvall, M. Sallander, A. Egenvall, U. Emanuelson, and A. Hedhammar, "A. Case-Control Study of Risk Factors for Canine Atopic Dermatitis Among Boxer, Bullterrier and West Highland White Terrier Dogs in Sweden," *Veterinary Dermatology* 18, no. 5 (2007): 309–315, https://doi.org/10.1111/j.1365-3164.2007.00617.x.
- 75. I. R. Dohoo, "Bias–Is It a Problem, and What Should We Do?," *Preventive Veterinary Medicine* 113, no. 3 (2014): 331–337, https://doi.org/10.1016/j.prevetmed.2013.10.008.

- 76. L. L. Baum, Y. Zablotski, K. Busch, and P. Koelle, "Reasons Why Dog Owners Stop Feeding Raw Meat-Based Diets (RMBDs)—An Online Survey," *Pets* 1, no. 1 (2024): 20–32, https://doi.org/10.3390/pets1 010004.
- 77. S. Gulec, G. J. Anderson, and J. F. Collins, "Mechanistic and Regulatory Aspects of Intestinal Iron Absorption," *American Journal of Physiology. Gastrointestinal and Liver Physiology* 307, no. 4 (2014): G397–G409, https://doi.org/10.1152/ajpgi.00348.2013.
- 78. L. M. Petje, S. A. Jensen, S. Szikora, et al., "Functional Iron-Deficiency in Women With Allergic Rhinitis Is Associated With Symptoms After Nasal Provocation and Lack of Iron-Sequestering Microbes," *Allergy* 76, no. 9 (2021): 2882–2886, https://doi.org/10.1111/all.14960.
- 79. C. F. Ramos, P. G. Doulidis, N. Polakova, et al., "Iron Deficiency in Dogs Suffering From Atopic Dermatitis," *BMC Veterinary Research* 20, no. 1 (2024): 506, https://doi.org/10.1186/s12917-024-04350-y.
- 80. Q. Wu, A. R. Carlos, F. Braza, et al., "Ferritin Heavy Chain Supports Stability and Function of the Regulatory T Cell Lineage," *EMBO Journal* 43, no. 8 (2024): 1445–1483, https://doi.org/10.1038/s44318-024-00064-x.
- 82. C. Stanescu, R. Talarico, S. Weichenthal, et al., "Early Life Exposure to Pollens and Increased Risks of Childhood Asthma: A Prospective Cohort Study in Ontario Children," *European Respiratory Journal* 63, no. 4 (2024): 2301568, https://doi.org/10.1183/13993003.01568-2023.
- 83. W. J. Zhu, H. X. Ma, H. Y. Cui, et al., "Prevalence and Treatment of Children's Asthma in Rural Areas Compared With Urban Areas in Beijing," *Chinese Medical Journal* 128, no. 17 (2015): 2273–2277, https://doi.org/10.4103/0366-6999.163381.
- 84. E. H. DeLucia, P. D. Nabity, J. A. Zavala, and M. R. Berenbaum, "Climate Change: Resetting Plant-Insect Interactions," *Plant Physiology* 160, no. 4 (2012): 1677–1685, https://doi.org/10.1104/pp.112.204750.
- 85. "IPCC 6th Assessment Report: Climate Change 2022: Impacts, Adaptation and Vulnerability," accessed May 15, 2025, https://www.ipcc.ch/report/ar6/wg2/.
- 86. S. Ardicli, O. Ardicli, D. Yazici, et al., "Epithelial Barrier Dysfunction and Associated Diseases in Companion Animals: Differences and Similarities Between Humans and Animals and Research Needs," *Allergy* 79, no. 12 (2024): 3238–3268, https://doi.org/10.1111/all.16343.
- 87. Y. Xing, M. H. Wang, T. F. Leung, et al., "Poultry Exposure and Environmental Protection Against Asthma in Rural Children," *Allergy* 77, no. 10 (2022): 2949–2960, https://doi.org/10.1111/all.15365.
- 88. F. Thoms, G. T. Jennings, M. Maudrich, et al., "Immunization of Cats to Induce Neutralizing Antibodies Against Fel d 1, the Major Feline Allergen in Human Subjects," *Journal of Allergy and Clinical Immunology* 144, no. 1 (2019): 193–203, https://doi.org/10.1016/j.jaci.2019. 01.050.
- 89. M. J. Jeger, A. Fereres, C. E. Malmstrom, K. E. Mauck, and W. M. Wintermantel, "Epidemiology and Management of Plant Viruses Under a Changing Climate," *Phytopathology* 113, no. 9 (2023): 1620–1621, https://doi.org/10.1094/PHYTO-07-23-0262-V.
- 90. R. W. Weber, "Current and Future Effects of Climate Change on Airborne Allergens," *Current Allergy and Asthma Reports* 24, no. 7 (2024): 373–379, https://doi.org/10.1007/s11882-024-01151-z.
- 91. L. H. Ziska, "Climate, Carbon Dioxide, and Plant-Based Aero-Allergens: A Deeper Botanical Perspective," *Frontiers in Allergy* 2 (2021): 714724, https://doi.org/10.3389/falgy.2021.714724.