



One Health: areas in the living environment of people and animals and their effects on allergy and asthma

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Summary

Background In a world with rapidly increasing urbanization and loss of closeness to nature and biodiversity, the question arises to what extent our environment influences the health of people and animals. Moreover, in recent decades, the prevalence of respiratory diseases such as asthma and allergies has risen sharply. In this context, a direct link between the health of people and their environment seems plausible.

Results Recent studies indicate that spending time in and being in contact with natural environments such as green spaces and associated soils is highly relevant to the health of people and companion animals. Green spaces in the environment of homes and schools of children and adults could contribute to the reduction of asthma and allergies. Especially the number and the structure of green spaces seems to be crucial. Home gardens and regular contact with animals can also reduce the risk of asthmatic and allergic diseases. In contrast, the increasing number of gray areas (roads, highways, construction sites, etc.) is likely to increase the risk of asthma and allergies. In the case of blue areas (rivers, lakes, sea), no correlation with atopic diseases has been found so far.

Conclusion Biodiverse green spaces, especially forests and meadows, may offer some protection against asthma and allergies. Contact with soil and ground

also seems important for the diverse skin microbiome, especially in childhood, and thus presumably beneficial for the immune system. Therefore, people and man's best friend, the dog, should spend sufficient time in green, biodiverse environments, despite—or perhaps because—of rapid urbanization. People should also actively create such biodiverse surroundings in their closer living environment. On a broader level, in the spirit of the One Health concept, those responsible for city planning and transportation must take these connections into account.

Keywords Atopy · Blue areas · Gray areas · Green areas · Sensitization · Urbanization

Abbreviations

BLG	Beta-lactoglobulin
BPDE-DNA	Benzo(a)pyrene diol epoxide DNA adducts
CAD	Canine atopic dermatitis
CORINE	Coordination of information on the environment
NDVI	Normalized difference vegetation index
RTSG	Ratio of trees to shrubs–grass
SPT	Skin prick test
SRI	Species richness index

The One Health concept

One Health is a concept that takes a holistic view on the health of people, animals, plants, and our environment. In this concept, problems are dealt with in an interdisciplinary way and by experts from many different fields and from different perspectives. It is also recognized that human health is closely related to a healthy state of the environment, vegetation, and animals. Typical problems, which also need to be addressed in a more interdisciplinary and holistic way,

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are asthma and allergy. The effects of changes in biodiversity, air and water pollution, emissions, global warming, urbanization, altered microbiome of people/animals/environment, application and remnants of medical substances, reduced exercise, processing of our food, nature of our living environment, and many more factors have to be considered. These factors can influence the development of allergy and asthma and must be included in the One Health concept when investigating causes, prevention, and, if necessary, treatment [1].

Factors influencing the development of asthma and allergy

The prevalence of asthma and allergies has risen sharply in recent decades. These diseases can represent a considerable restriction on the quality of life for those affected. The probability of developing allergy and/or asthma depends on endogenous as well as exogenous factors.

Genetics has a significant influence on both asthma and allergy, as the family history of these diseases is often reflected in the child [2]. It is estimated that the heritability of asthma ranges from 35 to 95% and of allergic rhinitis from 33 to 91% [3]. Thus, the probability that a child will develop asthma increases three-fold with one parent and six-fold with two parents being affected by asthma [4]. Nevertheless, it is unlikely that genetic factors alone have caused the rapid increase in diseases over the last few decades, and it is becoming increasingly clear that there must be an interaction between genes and the environment of the affected individuals [5, 6]. In this respect, cigarette smoke (passive and active), air pollution, growing up on a farm, contact with animals, but also diet, among others, may play a role [7]. Socioeconomic status, described by income, education, or occupation, also has a decisive influence because asthma and allergies can be very high in regions with poorer socioeconomic conditions [8, 9]. When genetic and socioeconomic factors have been included in the studies discussed below, they have been mentioned in Table 1.

Due to the ever-growing urbanization with the sealing of soil areas of our living, working, and school environment, human beings are losing contact with biodiversity and proximity to nature and wildlife [10]. This fact has negative consequences: people who live in urban areas with fewer green spaces are more likely to be affected by various immunological, metabolic, and mental diseases than those who live in rural areas [10, 11]. The question now arises, which and how many areas in our living environment can contribute to the protection against asthma and allergic diseases.

Green spaces: do they help protect against allergy and asthma?

Exposure to, and interaction with, green spaces and biologically diverse environments are associated with numerous benefits for physical and mental health [12–17]. Several studies show that green spaces influence the incidence of asthma and allergies; however, some of these provide mixed results (Table 1; [18]). The reason for this could be the heterogeneity of the settings in the studies conducted, as it probably depends on how (which measurement parameters), where (geographic location), and when (season, life stage of the subjects) the green spaces were assessed, and on other factors that may influence disease incidence but may not have been equally considered (e.g., pollen season, proximity to airports, highways, or farms) [2]. In addition to the size of the area, the structure as well as the characteristics of the green spaces seem to be of importance for asthma and allergy development [18–20].

Green spaces can represent both benefits and drawbacks for people and wildlife. One advantage is improved air quality, as increased green spaces of all types filter harmful particles and substances such as CO₂ and NO₂ from the air. Thus, green spaces can reduce lung exposure to harmful particles, thereby reducing asthma and allergy prevalence [18, 20].

As mentioned above, genetics also play an important role in the development of asthma. The influence of green space simultaneously with the genetic aspect was the focus of a research team from Toronto [18]. This city is home to a high number of ethnic populations and at the same time has a substantial variety of vegetation. According to the authors, the results are therefore suitable as a reference for affected ethnic populations in other countries. Green areas were measured by the ratio of vegetation components. For this, trees were surveyed separately from shrubs and grasses, and a ratio of these two groups was created. Using this ratio (“ratio of trees to shrubs–grass”), it was observed that a high ratio has a reducing effect on the incidence of asthma in 0–19-year olds. Furthermore, it was found that this effect can be enhanced by high tree diversity. A score for the density and diversity of street trees in the neighborhood was used as a parameter for tree diversity. However, such a positive effect could no longer be found for people over 20 years [18]. This discrepancy has been observed in several studies, and it was found that the influences of different factors can differ significantly among age groups. Even if the environment observed in the study is the same, it may still show different results on the incidence of asthma, as it seems that the effects may differ in different age groups and genders [21].

When comparing indoor with outdoor environments of 6–12-year olds in Budapest, children who lived in the suburbs had less asthma than those who lived centrally in the capital city [7]. The survey

Table 1 The effect of surfaces (green, blue and gray) on asthma and allergies in people

Type of area	Study	Age of the target group	Gender	Location	Setting	Period, survey methods and parameter	Readout parameters	Effect of the area on asthma or allergies
Green spaces	Molnar et al. 2021 [7]	6–12 years	Female and male	Budapest, Hungary	Residential and school area	Retrospective; 2019–2021; randomly selected elementary schools; one-time questionnaire for parents at baseline about children's symptoms in the past 12 months, previously physician-diagnosed asthma, food allergies, lifestyle, diet, and living environment (central city, suburban with greener areas); Socioeconomic effects not included; Genetic factors influenced by age and gender (asthma incidence less in girls than boys)	Prevalence of asthma	Living centrally in the city associated with higher risk of developing asthma than living in suburbia (OR = 2.13, CI: 1.36–3.24, $p = 0.0006$). Air pollution from heavy automobile traffic (OR = 1.29, CI: 1.05–1.59, $p = 0.0161$) and areas with grasses and weeds (OR = 1.39, CI: 1.15–1.69, $p = 0.0007$) were associated with higher asthma risk. Smoking: both contact in the first year of life (OR = 1.61, CI: 1.18–2.16, $p = 0.0018$) and at the time of study collection (OR = 1.65, CI: 1.24–2.18, $p = 0.0005$) as well as indoor mold (OR = 2.13, CI: 1.36–3.24, $p = 0.0006$) were associated with higher asthma risk. Keeping a rodent (OR = 0.72, CI: 0.52–0.98, $p = 0.0454$), and having a plant in the bedroom (OR = 0.79, CI: 0.65–0.96, $p = 0.0191$) were associated with lower asthma prevalence
	Roslund et al. 2021 [27]	3–5 years	Female and male	Finland	Kindergarten	Prospective; observation period of 2 years; questionnaires for parents to record use of antibiotics or other medication; Skin, saliva, and stool samples were collected (at baseline, day 28, 1 year, and 2 years); Socioeconomic effects were not included; Genetic factors considered by age and sex (taxonomic differences in saliva: girls had more <i>Prevotella</i> , <i>Veillonella</i> , and <i>Firmicutes</i>)	Microbiome of soil, skin, saliva and stool samples	Modified soils show constant accumulation of mycobacteria: (<i>Relative abundance in %</i>) Baseline: mean = 28 (SD = 10) vs. second year: mean = 74 (SD = 53) and Gammaproteobacteria : Baseline: mean = 63 (SD = 35) vs. second year: mean = 183 (SD = 164); Skin and saliva microbiome after 1 year: more gammaproteobacteria in intervention group than in standard group (<i>Presence/absence data</i>) Saliva: F-value = 3.790; $R^2 = 0.226$; P -value = 0.001; Q-value = 0.008; Skin: F-value = 2.341; $R^2 = 0.051$; P -value = 0.015; Q-value = 0.105
	Dong et al. 2021 [18]	0–19 and 20+	Female and male	Toronto, Canada	Toronto	Retrospective; 2016–2017; data from OCHPP; Vegetation was categorized using RTSG; Socioeconomic factors: – Income (household income correlated negatively with asthma in adults 20+, especially in women). – Household size (household size correlated positively with prevalence of asthma); Genetic factors: – Ethnic groups (results of the study are representative of other ethnic groups), – Different age groups – Gender (asthma in 0–19 year olds more in males, in over 20 year olds more in females)	Asthma prevalence	Green space structure with high tree diversity (high RTSG) is negatively associated with asthma in 0–19 year olds (coefficients of variables; outcome variable: prevalence of asthma = -0.27); no significant effect in 20+ year olds (-0.13)

Table 1 (Continued)

Type of area	Study	Age of the target group	Gender	Location	Setting	Period, survey methods and parameter	Readout parameters	Effect of the area on asthma or allergies
	Cavaleiro et al. 2021 [31]	0–7 years	Female and male	Portugal	Residential area	Prospective; observation period from birth to 7 years of the children, questionnaires for parents at 4 and 7 years of age to record symptoms and medical history of the children; Green area and species diversity were measured using NDVI and SRI; Socioeconomic effects such as: – Education of the mother – Number of persons in the household – Socioeconomic shortage are included in the evaluation as covariables Genetic factors: – Sex – Age were included in the study as covariables	Allergic sensitization, asthma, rhinitis, eczema	Children born in an area with a lot of green space have lower risk of having asthma at age 7 (OR [95% CI] = 0.41 [0.18 : 0.97]); But when only species richness (SRI) is considered: higher SRI leads to significantly higher risk of allergic sensitization at age 4 years (OR [95% CI] = 2.00 [1.04 : 3.86]) and at age 7 years (OR [95% CI] = 2.35 [1.20 : 4.63])
	Paciencia et al. 2021 [20]	0–10 years (+ mothers)	Female and male	Portugal	Residential area	Prospective; interviews and questionnaires for parents at baseline: questions about home environment, lifestyle, illnesses; re-evaluation at 4, 7, and 10 years; Allergic sensitization to food and aeroallergens was tested in serum samples from children aged 10 years as specific IgE antibodies (ImmunoCAP fx1 nut mix, fx22 nut mix, Phadiatop Infant); (one or more allergens ≥ 0.35 kU/L); Vegetation classified using NDVI; Socioeconomic factors: – Mother's education , – Number of household members were included in the calculation models—the included children all came from similar socioeconomic backgrounds (high educational status, lower number of people in the household); Genetic factors: – Sex – Ages were included in evaluation	Allergic sensitization	More green space near the residential area at the age of 10 (HR [95% CI] = 0.095 [0.011, 0.823]; adjusted for socioeconomic factors) and higher lifetime exposure leads to lower risk of allergic sensitization HR (95% CI) = 0.539 (0.301, 0.965)
	Dzhambov et al. 2021 [2]	8–12 years	Female and male	Austria and Italy	Residential and school area	Retrospective; 2004–2005; questionnaire for mothers on allergic symptoms, asthma symptoms, lifestyle, and household conditions; Vegetation determined using NDVI and tree canopy cover; Socioeconomic factors: – Persons in household – Education of the mother Genetic factors: – Sex – Age were included in evaluation	Asthma, allergy, allergic rhinitis and eczema	Fewer asthma and allergy symptoms in children with more green spaces – In the residential environment (marginal association): * NDVI: current asthma OR 0.80 (CI 0.63, 1.02), ever allergic rhinitis: OR 0.83 (CI 0.67, 1.03); * tree cover: asthma OR 0.86 (CI 0.66, 1.12), rhinitis: OR 0.86 (CI 0.68, 1.09). – In the school environment (p -value < 0.05): * NDVI: rhinitis OR 0.86 (CI 0.74, 0.99); * tree cover: rhinitis OR 0.73 (CI 0.57, 0.94). – Owning a home garden (minimally adjusted associations; p -value < 0.05): asthma OR 0.69 (CI 0.50, 0.96). – More outdoor time : asthma OR 0.73 (CI 0.54, 1.00)

Table 1 (Continued)

Type of area	Study	Age of the target group	Gender	Location	Setting	Period, survey methods and parameter	Readout parameters	Effect of the area on asthma or allergies
	Aerts et al. 2020 [23]	6–12 and 13–18 years	Female and male	Belgium	Residential area	Retrospective; sales of medication for COPD in 2010–2014 were used to determine asthma prevalence; Land cover and different types of green areas taken from the topographic database “Top10Vector”; Socioeconomic effects on respiratory health were not included in study (cited as a limitation); Genetic factors were determined by – Age and – Gender (medication sales highest among 6- to 12-year-old boys) included in statistics	Asthma	Proximity to grasslands and range-lands negatively affects (increases) asthma medication sales; Unadjusted parameter estimates per IQR increase of relative cover, range across four strata: 6- to 12-year-old girls, $\beta = 0.088$, 95% CI: 0.069–0.107; 6- to 12-year-old boys, $\beta = 0.071$, 95% CI: 0.048–0.094; 13- to 18-year-old boys, $\beta = 0.090$, 95% CI: 0.071–0.109 (all $p < 0.001$); Also home gardens showed negative effect on respiratory health (corrected for house quality and chronic air pollution): $\beta = 0.07$ –0.09; Forest area: 13- to 18-year-old girls a small protective effect. (Sale of asthma medication vs. forest area $\beta = -0.013$, 95% CI: -0.025 to 0.000, $p = 0.048$)
Gray areas	Maio et al. 2021 [40]	15–84 years	Female and male	Italy	Residential area	Retrospective; 1991–1993; survey by questionnaires: asthma symptoms or diagnosis, allergic rhinitis (symptoms or diagnosis); Blood test: biomarker for allergy as well as for benzo(a)pyrene exposure; IgE values and skin prick test for 12 allergens (pollen, dust mite, mold, animal dander); Gray areas around the residential area of the study participants were surveyed by CORINE framework (Europe-wide satellite system measuring land cover); for each participant in 1000 m radius the different land cover types around the residential area were measured; Socioeconomic factors: – Number of persons in household – Family history asthma and allergy – Education (70.6% had low level of education) Genetic factors: – Age – Sex – BMI Factors included in evaluation models	Asthma, allergy, allergic rhinitis	More gray area led to significantly higher probability for – Positive skin prick test (OR 1.07, 95% CI 1.02–1.13), – Polysensitization (OR 1.11, 95% CI 1.04–1.19), – Rhinitis (OR 1.10, 95% CI 1.04–1.17) as well as – Only asthma or allergic rhinitis (without SPT positivity) (OR 1.06, 95% CI 1.00–1.12); 10% increase in individual exposure to gray areas associated with higher incidence of skin prick test positivity and asthma and allergic rhinitis (OR 1.16, 95% CI 1.08–1.25)
	Dzhambov et al. 2021 [2]	8–12 years	Female and male	Austria and Italy	Residential and school area, Brenner Pass	Retrospective; 2004–2005; questionnaire for mothers on allergic symptoms, asthma symptoms, lifestyle, and household conditions; Vegetation was determined using NDVI and tree canopy cover; Socioeconomic factors: – Persons in household – Education of the mother Genetic factors: – Sex – Age were included in evaluation models	Asthma, allergy, allergic rhinitis and eczema	Gray area (500 m around home and school area) associated with more severe symptoms of asthma and allergy OR 1.30 (CI 1.00, 1.68) (p -value < 0.05)

Table 1 (Continued)

Type of area	Study	Age of the target group	Gender	Location	Setting	Period, survey methods and parameter	Readout parameters	Effect of the area on asthma or allergies
	Tischer et al. 2017 [39]	0–4 years	Female and male	Spain	Residential area	Prospective; questionnaires for parents of 4-year-old children in the INMA birth cohort on symptoms of allergy, bronchitis, allergic rhinitis, and asthma; Birth cohort lives in two different biogeographic regions: Euro-Siberian region and Mediterranean region; Cover types determined by NDVI, proximity of residential areas to green space, and gray of residential environment (using CORINE program); Socioeconomic factors: – Education status of the mother – General socioeconomic status (according to the “urban vulnerability index”); Genetic factors: – Age – Sex aORs were corrected using these factors	Respiratory health, bronchitis, rhinitis	Higher number of gray space near residential area (300 m) led to borderline increased risk of wheezing aOR 1.29 (CI 95% 0.98–1.70) and bronchitis aOR 1.58 (CI 95% 1.19–2.08) at the age of 4 years in the Mediterranean region
Blue areas	Paciencia et al. 2021 [20]	0–10 years (+ mothers)	Female and male	Portugal	Residential area	Prospective; interviews and questionnaires for parents at baseline: questions about home environment, lifestyle, illnesses; re-evaluation at 4, 7, and 10 years; Allergic sensitization to food and aeroallergens in serum samples from children aged 10 years tested for specific IgE antibodies (ImmunoCAP fx1 nut mix, fx22 nut mix, Phadi-atop Infant) (= one or more allergens ≥ 0.35 kU/L); Vegetation was determined using NDVI; Socioeconomic factors: – Mother's education, – Number of household members included in calculation models—the included children were all from similar socioeconomic backgrounds (high educational status, lower number of people in the household); Genetic factors: – Sex – Ages were included in evaluation models	Allergic sensitization	No significant association between distance to nearest blue area and allergic sensitization at age 10 years

aOR Adjusted odds ratio, CI Confidence interval, COPD Chronic obstructive airway disease, CORINE Coordination of Information on the Environment, HR Hazard ratio, IgE Immunoglobulin E, INMA Infancia y medio ambiente birth cohorts, NDVI Normalized difference vegetation index, OCHPP Ontario Community Health Profiles Partnership, OR Odds ratio, RTSG Ratio of trees to shrubs–grass, SD Standard deviation, SPT Skin prick test, SRI Species richness index

was conducted in 21 schools with questionnaires distributed to the children's parents to determine whether they had asthma or had already been diagnosed by a doctor, and to assess the children's symptoms (wheezing, breathing noises), living environment, lifestyle, and diet. This study showed that air pollution from heavy automobile traffic and areas with grasses and weeds were associated with a higher risk of asthma. Indoors, smoking (both, contact during the first year of life and at the time of the survey between the ages of 6 and 12 years of age) and molds were identified to increase asthma, while having a pet

rodent or a plant in the bedroom was associated with lower asthma risk. Children's regular physical activity significantly reduced respiratory symptoms [7].

A study investigated the association between landscape characteristics and allergic symptoms in 8–12-year olds in Austria and Italy [2]. For this purpose, data of the Wipptal and the Unterinntal and their neighboring valleys were collected. These valleys are characterized by their rural environment, but are located close to the traffic-busy Brenner Pass. This unique environment, characterized by strong vegetation and biodiversity, coexists with a high level of exhaust gases. The

evaluation of green and gray area indicators around the residential area (100, 500, and 1000 m) and the children's school area (100 m) showed that the prevalence of asthma and rhinitis decreases with increasing green area. The prevalence of asthma also decreases when the children have a residential garden and spend more time outdoors. On the other hand, when there was a decrease in green space within a 500 m radius of the children's residential area, the prevalence of asthma increased. A higher number of green spaces also correlates with lower NO₂ exposure and, consequently, a lower prevalence of asthmatic symptoms [2].

However, many of the studies mentioned above have only looked at the effect of green space at a specific time in children's lives. Observing the effect of green spaces on children for 10 years, it was described that those who had more green spaces in their living environment during their lifetime (500 m) were less likely to develop allergic sensitization [20]. The authors suggest that children are more encouraged to play in the fresh air in green areas and, thus, have more interaction with these areas and soils [20]. There seems to be a specific window of opportunity in childhood when it is important to spend much time in as diverse a natural environment as possible, with trees and green spaces, to provide some protection against asthma and allergies.

Contrary to all the studies that could show that green spaces have positive effects on health, some found a negative association. Green spaces produce pollen, which can trigger allergic symptoms [18, 22]. In combination with other factors such as air pollution, fungal spores, or endotoxins, these can result in respiratory diseases. In one study, asthma medication sales were compared with three different types of green spaces (forest, grassland, and home garden) in the residential environment [23]. As one of the strengths of this study, the effects of the different types of green spaces were observed separately for gender and two different age groups (6–12 years and 13–18 years). In contrast to the positive effects described above, it was shown here that proximity to large areas of grasses or pastures could have a detrimental effect on children's respiratory health and associated medication use. It was found that home gardens can also adversely affect children's respiratory health, as in this case children are exposed to a variety of pollens and molds. In the group of 13- to 18-year-old girls, a small negative association was found between asthma medication sales and forest areas [23]. A meta-analysis of nine studies showed that a 10% increase in green space was significantly associated with a 5.9–13% increase in wheezing, asthma, and allergic rhinitis, but not eczema [24].

However, not only the green spaces themselves but also the associated soil contributes to the resulting effects. In general, sufficient contact with a natural environment is important because this contact enriches

the human microbiome, which may improve immune balance, potentially protecting against allergies and inflammatory diseases (biodiversity hypothesis) [25, 26]. With the decrease of green areas, contact with soil and earth is disappearing progressively, and with it the influence on our microbiome. The influence of soil has been researched by modifying soils in kindergartens, which were enriched with turf and forest soil [27]. Furthermore, boxes for planting were provided to the children to enable active handling and contact with soil. One of the changes that could be shown over the observation period of 2 years was an enrichment of the soil microbiome with the genus *Mycobacteria*, which in the literature are said to have anti-inflammatory properties [28]. Very few to no mycobacteria were detected in the soils of standard nurseries without intervention. The authors speculate that the higher proportion of *Mycobacteria* in the soils may benefit children's immune regulation, but further studies are needed. The microbiome in skin and saliva samples of the children showed more Gammaproteobacteria after one year of observation. Gammaproteobacteria were also found to increase after 2 years in the soil of the kindergartens with modification, but not in the standard kindergartens. This result also correlates with a higher diversity of this particular class of bacteria in the children's skin and saliva samples. Higher numbers of Gammaproteobacteria in the soil and the skin microbiome have been associated with ideal immune modulation and already in the past with reduced risk of atopy and allergies [29, 30]. In parallel, fewer *Haemophilus parainfluenzae*, *Streptococcus sp.* and *Veillonella sp.* were found in the samples of children with modified soils compared to the control nurseries. These strains have been consistently associated with childhood asthma [27]. Therefore, by enriching the outdoor environment and soils in kindergartens, there is an opportunity to positively impact the microbiome and even reduce potential pathogens in the environment.

Not only green spaces and the respective soil but also the specific plant species growing in them are of interest for the development of asthma and allergy. A study from Portugal compared how the number of green spaces (normalized difference vegetation index, NDVI) and the number of plant species growing in them (species richness index, SRI) affected children [31]. Genetic as well as socioeconomic factors were also included in the statistical analysis of the study. Individuals who had physician-diagnosed allergy, rhinitis, or eczema were considered to have an allergic disease. The same was true for asthma. Those children who lived in areas with a high number of different plant species in the green areas (100 m around the residential area) had a significantly higher risk of suffering from allergic sensitization than children from regions with smaller species diversity: at the age of 4 years, the risk increased on average two-fold and at the age of 7 years even 2.4-fold. The authors ex-

plain this result by the fact that a higher number of species also brings a greater amount of plant-associated aeroallergens and consequently more symptoms for those affected. However, when only the “size of green space” factor was considered, this study was also able to show that children born in neighborhoods with a high proportion of green space (100 m around residential areas) had a lower risk of suffering from asthma at the age of 7 years and a lower prevalence of allergic rhinitis than children growing up in neighborhoods with little green space [31].

A special case for a protective environment against asthma and allergies for human beings and animals is provided by farms that induce the so-called farm effect. Here, not only the direct contact to cattle and the consumption of raw milk [32] but also the dust of the barn up to a distance of 300 m around the barn seems to be effective [33]. Our research group was able to show that an effective component in barn dust and ambient air—in addition to the good microbes and their components—is the milk protein beta-lactoglobulin (BLG). BLG is a carrier protein and, together with its ligands (vitamins, iron-siderophores, zinc), can positively modulate the immune system [34–37].

Gray areas: Does gray make us sick?

In addition to green spaces, increasing gray areas, such as larger cities and more roads or highways, are also of interest in allergy and asthma research (Table 1). Evidence is mounting that higher levels of gray areas, such as asphalt, correlate with allergies and respiratory health. A Finnish study was able to show that asphalt use increased ten-fold over three decades (1960–1990). A parallel and similar increase was found in the same paper for asthma prevalence in conscripts. This increased from 0.3% (1966) to 2.6% (1995) [38]. To measure the influence of gray areas near where children live (300 m), the CORINE (“Coordination of Information on the Environment”) program was used in a study [39]. Industrial, commercial, and transportation units were included, as well as mines, landfills, and construction sites. Furthermore, birth cohorts from two different biogeographical regions in Spain were compared. It was found that more gray areas around the residential area increase the risk of wheezing as well as bronchitis in children [39]. Also, in a study for adults (15–84 years), the CORINE program was used to measure the different land cover types around the residential area (1000 m) of the study participants [40]. The mean gray area percentage within a 1000 m radius of the study participants’ residential area was 46.52%. About one-third of the probands (32.8%) lived in areas with a gray area percentage of 31–40%, and 17.1% lived in areas with even 81–90% gray area percentage. Individuals with biomarkers for allergic diseases as well as individuals with serum antibodies against benzo(a)pyrene-diol-epoxide (BPDE) DNA adducts (as markers for

exposure to environmental carcinogens as well as DNA damage) were found to have the highest levels of gray area exposure. Furthermore, a significantly higher probability was found for a positive skin prick test (SPT), polysensitization, rhinitis as well as only asthma or allergic rhinitis (without SPT positivity). A 10% increase in individual exposure to gray areas was associated with a higher incidence of SPT positivity, asthma, and allergic rhinitis. Thus, this study could describe a possible negative effect of gray areas [40]. In the study mentioned above, which investigated rural valleys but had the traffic-busy Brenner Pass nearby, it could be shown that a higher density of gray areas leads to an increase in asthma symptoms [2]. This effect is probably due to exhaust fumes from cars and the lower amount of filtering green areas. These results are not surprising since air pollution is a known asthma-amplifying factor. Since the number of studies on gray areas and asthma/allergy is very small, further studies need to clarify a direct causal effect.

Blue areas: Can water be helpful?

Comparing green areas and water areas such as lakes and rivers (Table 1), it was found that there was no significant association between water areas close to the residential area (500 m) and allergic sensitization in children after an observation period of 10 years [20]. A European study of 3- to 14-year-olds also failed to find a correlation between blue areas (bodies of water, coastal lagoons, estuaries, and the sea) in the living environment and allergic symptoms [24]. However, to be able to make an accurate statement about the effects of blue areas on allergy and asthma, further studies are necessary.

Are our pets also affected?

Our pets can also develop asthma and allergies [41–43]. A highly prevalent allergic skin disease in dogs is canine allergic dermatitis (CAD). It affects approximately 10–15% of the canine population and is a genetically predisposed allergic skin disease with itchy and inflamed skin areas. Since the number of cases of CAD has increased sharply in recent decades, it can be assumed that, as in humans, environmental factors may also play an important role ([44]; Table 2). Accordingly, dogs living in a city suffer more often from CAD than those living in rural areas. Regular walks with the dog in the forest seem to be particularly effective. The coexistence of the dog with other dogs or cats protects likewise [44]. A similar observation is made in humans, where a higher number of family members and living with pets is protective [45].

It has also been shown that people have different contact with green spaces and that those with pets, such as dogs, spend more time in them than others

Table 2 The effect of green spaces on allergies in owners and their dogs

Study	Animals	Number of animals	Location	Design/Setting	Readout/Parameter	Effect
Lehtimäki et al. 2020 [47]	Dogs (+ owner)	168 dog owner pairs	Finland	Prospective; urban vs. rural setting	Skin and fecal samples from dogs and humans, questionnaire to owners about allergy symptoms in dogs and humans; Breed, sex, allergy of the mother-dog, living environment and sensitization of the owner were included in the statistical evaluation	31% of couples with common living environment as well as lifestyle sensitized to aeroallergens (mean sum specific IgE = 15.30 kU/l, range = 1.02, 78.94); Urban dogs are more likely to suffer from allergy symptoms than rural dogs (logistic regression; $p = 0.003$); In humans, similar but borderline correlation was found (logistic regression; $p = 0.054$); Living in city increases allergy risk in dogs (logistic regression, $p = 0.007$); not statistically significant in humans (logistic regression, $p = 0.093$); Owner and dog suffer from allergy at the same time (logistic regression, $p = 0.002$), and this more in urban environment (ANOVA, $p = 0.01$) and urban lifestyle (ANOVA, $p = 0.028$) than in rural
Hakanen et al. 2018 [48]	Dogs (+ owner)	5722 dogs	Finland	Retrospective; city vs. rural environment	Questionnaire to owners about allergy symptoms in dogs and humans: Skin symptoms such as itching/scratching, redness, eczema; Respiratory symptoms such as cough, rhinitis; Eye or ear infections; Gastrointestinal symptoms such as diarrhea, vomiting, constipation, etc.	Current urban residence had a higher risk of allergy (logistic regression OR = 1.24, $p = 8.3e-07$); Regular contact with other animals (farm animals $Z/X^2 = 9.96$, $p = 0.007$ and pets $Z/X^2 = 7.85$, $p = 4.10e-15$) protects both dogs and humans from allergic symptoms
Meury et al. 2011 [44]	Dogs	378 dogs	Switzerland and Germany	Retrospective; place of living in general	Canine atopic dermatitis (CAD)	Living in city increases frequency of CAD (OR = 2.67, $p = 0.002$). Regular walks in the forest (OR = 0.41, $p = 0.006$) show protective effect on CAD

CAD Canine atopic dermatitis, IgE Immunoglobulin E, OR Odds ratio

[46]. Therefore, it is not possible to individually assess the sole effect of different types of land cover, such as green spaces, from the numerous other factors that may affect asthma as well as allergy in owners and dogs.

It is very exciting that dogs and their owners who live in the same environment and have the same lifestyle show the same allergy prevalence: They are often healthy or show allergic symptoms at the same time. Of tested dog–owner pairs who share their living environment and lifestyle, 31% show sensitization to aeroallergens [47]. Another observation shows that a sensitized owner was more likely to have a dog that was sensitized than to have a healthy dog. There is a high probability that this effect is due to common underlying environmental and lifestyle factors [48]. To confirm this, the different microbial compositions of the environment of holders and dogs and their effects on the skin and gut microbiome were investigated. By analyzing skin and fecal samples from dog–owner pairs, it was shown that the gut microbiome is clearly different while the skin microbiome is similar and that the skin microbiome of dog–owner pairs is more similar than that of random dog–human pairs. A link between skin microbiome and lifestyle and living environment in dogs and holders was also found. Thus, a potentially important role of microbial exposure, lifestyle, and environment in the risk of allergy can be assumed. Since these results have been found in dogs and people, it is very likely that immune-related diseases may also have common environmental origins [47].

Discussion

The associations found in the as yet few studies show good correlations, but do not yet prove causality of the different areas in asthma and allergy development. Further studies—preferably prospective intervention studies—are needed. However, the existing studies support the hypothesis that environmental factors and surroundings, such as green spaces, among others, may support asthma and allergy prevention. Asthma and allergy are complex and multifactorial diseases, and the influence of green spaces can therefore only be one aspect among many.

In the sense of the One Health concept, it would be advantageous for necessary future studies to deal with questions in an interdisciplinary manner. It would also be desirable to include existing and new results in future urban planning in order to ensure better health for all. Therefore, the working group One Health of the EAACI (European Academy of Allergy and Clinical Immunology) is dedicated to these topics and their practical implementation.

Conclusion

The work described shows correlations, but does not necessarily prove causality. Nevertheless, different results were found for gray, blue, and green areas: Gray areas could contribute to the development of asthma and allergies, blue areas have no influence as far as known so far, whereas trees, green areas, and soil with high biodiversity seem to protect against asthma and

Fig. 1 Effect of areas on the prevalence of asthma and allergies. Different areas probably influence the development of asthma and allergy in different ways. While *gray* areas (roads, highways, construction sites, etc.) could have a negative impact on the respiratory health of people and dogs, and no correlation has yet been found for *blue* areas (rivers, lakes, sea), *green* areas (parks, forests, grassland, and home garden) apparently offer a protective effect

Risk for asthma, allergy and atopy



allergy development in people and animals (Fig. 1). In this sense, the way of cultivation and remodeling as well as the construction of the living environment as a holistic approach of the One Health concept [1] is an important contribution to the reduction of the “allergy pandemic” and these results should be incorporated into city planning in the future.

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Conflict of interest K. Zednik and I. Pali-Schöll declare that they have no competing interests.

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