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Review

Aeroallergens in Canada: Distribution, Public Health Impacts, and Opportunities for Prevention

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Abstract: Aeroallergens occur naturally in the environment and are widely dispersed across Canada, yet their public health implications are not well-understood. This review intends to provide a scientific and public health-oriented perspective on aeroallergens in Canada: their distribution, health impacts, and new developments including the effects of climate change and the potential role of aeroallergens in the development of allergies and asthma. The review also describes anthropogenic effects on plant distribution and diversity, and how aeroallergens interact with other environmental elements, such as air pollution and weather events. Increased understanding of the relationships between aeroallergens and health will enhance our ability to provide accurate information, improve preventive measures and provide timely treatments for affected populations.

Keywords: aeroallergens; pollen; fungi; allergy; asthma; atopic march; Canada

1. Introduction

Over the past 70 years, the prevalence of allergic conditions has increased in high-income countries to the point of becoming a worldwide public health concern [1]. This increase cannot be explained by genetic changes only [2]. Environmental exposure to air pollutants and aeroallergens have been hypothesized as potential causes for this steep increase, as the nature of these exposures have changed during a similar window of time [3].

Environmental factors play a key role in defining the type of sensitization and the kind of atopic disease in genetically at-risk individuals. While heredity regulates the intergenerational transmission of the susceptibility to different phenotypes of atopic responsiveness, environmental exposure is a crucial factor in the development of atopic disease. The environmental exposures linked to the development

of allergies are to: (a) common aeroallergens (e.g., pollen or mold spores); and (b) pollution, like particulate matter (PM) or environmental tobacco smoke (ETS), among others [4].

The environmental exposures listed produce a specific imbalance in the immune system [5]. There are two types of T helper immune cells (Th1 and Th2) that appear imbalanced in allergic conditions [6], with a higher proportion of the Th2 cell population [7]. The hygiene hypothesis is also considered as one of the reasons for the specific imbalance in the immune system [8]. This hypothesis attributes a reduced exposure to infectious agents at key times of immune system development to the Th2 predominance. This skewed microbial exposure may be due to improved hygiene and sanitation, and increased use of disinfectants and antibiotics [9]. When an individual has this type of imbalanced immune system, repeated exposures to a myriad of specific proteins (e.g., pollen, certain molds, dust mite feces, eggs, peanuts) can induce the creation of IgE antibodies [10]. These initial encounters with the proteins produce a sensitization to these specific molecules, and subsequent exposures will trigger symptoms each time [10,11].

Allergy symptoms in response to pollen and fungal spores are driven by IgE that is specific to proteins found in these spores [12]. The allergenicity of pollen spores refers to the concentration of protein epitopes in each spore, to which specific IgE molecules produced by the plasma cells of allergic individuals may bind [13]. Certain pollen grains are known to be highly allergenic (e.g., ragweed a.k.a *Ambrosia*), and highly prevalent in some parts of Canada [14]. This combination of allergenicity and prevalence makes some ambient aeroallergens highly problematic due to the growing number of exposed and sensitized individuals [15]. This exposure and the physical symptoms of the immune response have a direct impact on the everyday lives of patients with allergic conditions. They also have an impact at the societal level, including costs to the health systems that address medical needs associated with allergic responses.

This review will describe the current state of our knowledge about the variety and distribution of plant and fungi-derived aeroallergens in Canada. We will also discuss allergic diseases and the health impacts that Canadian allergy sufferers experience in connection with aeroallergens and the weather and climatic conditions that enhance exposure. It is our hope that this public health-oriented review will enhance the ability of researchers, health practitioners, and governments to provide accurate information to the public and improve preventive measures and treatments.

2. Review

2.1. Introduction to Ambient Aeroallergens

Pollen grains function as a container for the male gametophytes of plants [16]. The essential reproductive event among higher plants is achieved only when the pollen grain is successfully transferred from the floral anther to the recipient stigma. The strategies that plants use in their pollen transfer are classified into two categories: entomophilous plants depend on organisms such as insects or hummingbirds to carry larger, stickier pollen grains, anemophilous plants release large quantities of pollen grains to be blown in the wind [17].

When anemophilous plants release pollen, a number of environmental factors affect how, when, and how many grains reach their final destination [18]. The aerobiology pathway of pollen (as seen on Figure 1) illustrates how pollen grains can travel from their source to interact with humans and potentially affect health. Many of these factors are affected by shifting climatic conditions [19,20].

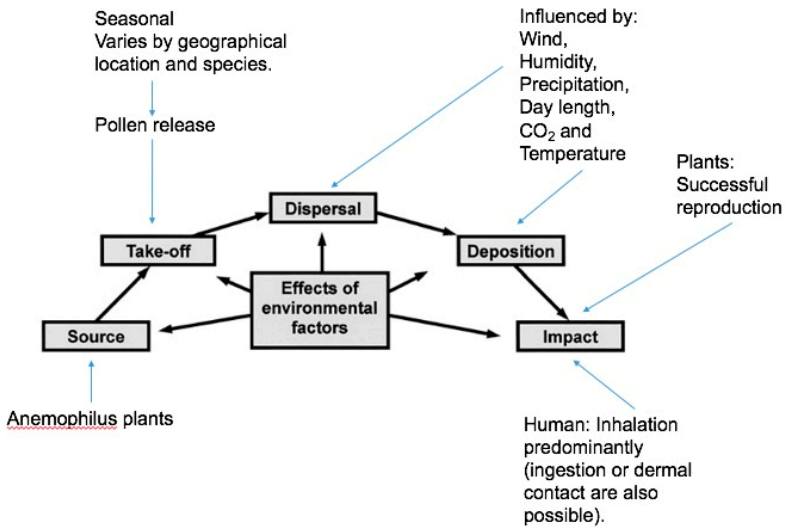

Figure 1. The aerobiology pathway of pollens, adapted from [21].

Currently, more than 150 pollen allergens are curated by the International Union of Immunological Societies [22]. From the entire list of pollen allergens, 12 are of particular interest in Europe due to their abundance in the atmosphere [23] and allergenic potency [24] (p. 10): (1) ragweed (*Ambrosia*); (2) alder (*Alnus*); (3) mugwort (*Artemisia*); (4) birch (*Betula*); (5) goosefoots (*Chenopodiaceae*); (6) hazel (*Corylus*); (7) cypresses, including yews (*Cupressaceae/Taxaceae*); (8) olive (*Olea*); (9) plane tree (*Platanus*); (10) grass (*Poaceae*); (11) oak (*Quercus*); (12) and wall pellitory (*Urtica/Parietaria*).

In Canada, birch and grasses are more abundant than ragweed, which is found mostly in Ontario and Quebec. Cypress, olive, plane tree, and wall pellitory are not present in Canada [14].

2.2. Canadian Distribution of Plant-Derived Aeroallergens

The geographical distribution of species of plants is dependent on multiple factors, including precipitation, soil composition and moisture and average high and low temperatures [14]. Five "floristic zones" that support the growth of different aeroallergen-producing plants have been defined across Canada [14]. As seen on Figure 2, from west to east, they are: Northwest Coastal, Northern Forest, Rocky Mountain, Central Plains, and Eastern Agricultural [14]. The major allergenic plants that grow in each of the floristic zones are widely varied (Table S1 in the supplementary materials).

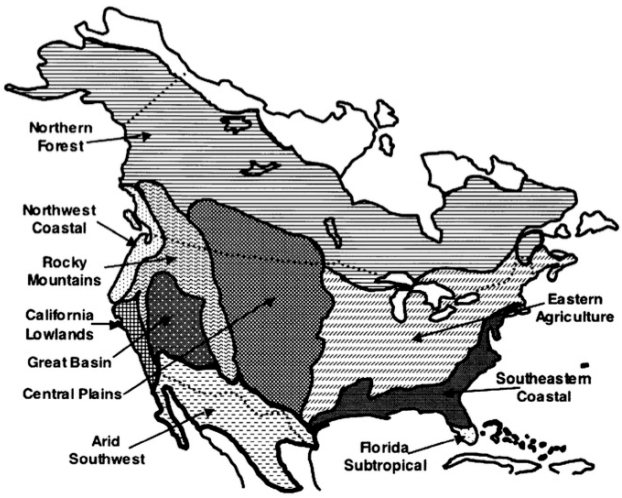

Figure 2. Floristic zones of North America, from [14].

Trees, grasses, and ragweed are the most common allergens associated with outdoor pollen-induced allergies across Canada [25–27]. Short ragweed is highly cross-reactive with all other ragweed species, as well as sage and mugwort [25,26,28–30]. Additionally, there is substantial clinical cross-reactivity between tree and grass allergenic species [27]. For example, individuals allergic to birch pollen in Northern Sweden have also been sensitized to beech pollen (*Fagus*), although that species does not grow in the region [31].

Local factors can affect spatial variation within a region [32]. Examples of the local factors are: tree canopy, defined as the types of trees planted in the geographical area of interest [33]; and level of urbanization, defined considering street network coverage and quantity of vegetation [34]. The amount of pollen in the air at a particular location depends on the distance and number of source plants in the area, atmospheric conditions and plant physiological factors such as the number of accumulated degree days at which their pollen is released [35]. Pollen grains can break open to release submicronic pollen-derived bioaerosols containing allergenic proteins, particularly when the grains have been aloft for some time and/or become wet [36–39] as in thunderstorm asthma. Some increased exposure to aeroallergens is also due to human activity, such as landscaping practices that create niches favoring the growth of weeds such as ragweed [35].

2.3. Fungal Aeroallergens

Fungi are eukaryotic organisms that grow all over the world, in the presence of moisture and carbohydrates [40,41]. Currently, fungi are organized into eight phyla, three of which produce important aeroallergens: (1) *Zygomycota*; (2) *Ascomycota*; and (3) *Basidiomycota* [41–43]. Fungi produce spores on maturity, through both sexual and asexual mechanisms [44,45]. The asexual spores produced by mitosis appear to be the most allergenic [41,46]. In addition to molecules on the surfaces of spores, fungi also secrete enzymes into their environment that can act as allergens in sensitized individuals [41,47]. Fungi spores have low mass and can remain suspended in the air for varying periods of time depending on the weather [48]. Outdoor airborne fungi such as *Cladosporium*, *Alternaria*, *Penicillium*, and *Aspergillus* can trigger allergic responses in sensitized individuals [49].

2.4. Aeroallergen Measurement and Prediction

Outdoor aeroallergen sampling is largely based on microscopic examination to identify pollen and spores based on morphologic pattern recognition [50,51]. Aeroallergens must be collected and then manually counted, so it is impossible to generally offer real-time data using these methods. Furthermore, it is not yet feasible to provide dense spatial coverage or to offer sub-daily counts on a regular basis, although bi-hourly values are occasionally reported in research [52].

Aeroallergen count modeling and forecasting allows for more detailed maps that provide estimates for locations other than sampling sites. This requires knowledge of botanical and meteorological data over several years to assess the variations possible in seasonal pollen characteristics [53]. Land use regression (LUR) modelling is a mapping technique [33] that has been used to explain approximately 79% of the spatial variation in pollen measurements [54]. Results from LUR models are a potential source of relevant information for epidemiologic studies of allergic conditions [33]. Model improvements and their validation by additional local measurements are needed to provide more accurate maps and forecasts for epidemiologic studies and to help allergic individuals and their health care providers reduce the burden of illness [53].

2.5. Aeroallergen Impact on Humans

Pollen grains carry noninfectious proteins, so exposure to pollen is an innocuous event for most individuals [55]. For others, however, it triggers an allergic immune response and related symptoms. In recent decades, pollen allergy has grown increasingly prevalent, affecting as much as 40% of the population in regions of Australia, New Zealand, and the United States, and becoming widely recognized as a public health concern [56].

Because the primary mode of dispersal for pollen grains and fungi spores is via the air, humans are exposed predominantly through inhalation [57]. The respiratory system is the first point of contact between the human body and the proteins contained in pollen and fungi [48], and that is where inflammation takes place following exposure to allergens [58]. Allergies are diagnosed using 'skin-prick tests', which demonstrate the presence of a Type I hypersensitivity, involving IgE, at a site on the skin where a small amount of allergen is introduced through a 'prick' [22,59]. For seasonal allergic rhinitis, grass, and tree pollens are the most common allergens [60].

The point at which aeroallergens impact on the respiratory system depends on their size. Aeroallergen size can vary from less than 10 μm to 100 μm, and can be classified into the following groups: very small (<10 μm), small (10–25 μm), medium (26–50 μm), large (51–100 μm), and very large (>100 μm) [61]. According to Szema [62], aeroallergen grains larger than 5 μm deposit in the ocular conjunctiva and nasal mucosa and have the potential to trigger allergic reactions such as conjunctivitis or allergic rhinitis [2,63], and also to asthma exacerbation [64]. Smaller particles than <5 μm, come from allergens such as cat dander, can reach the lungs, and have been linked to asthma onset [65].

2.6. Aeroallergens and the Development of Respiratory Allergies

Worldwide, a steep increase in the prevalence of Type I hypersensitivity reactions—such as asthma and allergies—has been documented in every age group [66]. Recent studies report significant differences over such a short timespan that the findings cannot be explained by genetic changes [67–70]. Better understanding of the environmental factors that affect the development of atopic disorders and their phenotypic expression could lead to better understanding of their increased prevalence. Because pollen grains from anemophilous plants are one of the most important allergen sources in the outdoor air [57], their role in development of asthma and allergy needs further exploration. Spores from fungi are also important aeroallergens that have been linked to allergic reactions [41,46] and in some studies potentially also to the risk of asthma development [71].

Asthma is one of the most severe expressions of an adverse immune response in the respiratory system [72,73]. Moreover, researchers such as de Weger et al. [58] and von Mutius [74] acknowledge the diversity of factors that influence the health impact of aeroallergens and call for better understanding of the extrinsic influences and intrinsic factors that contribute to the new onset of the allergic conditions associated with aeroallergen exposures. Among the possible explanations for the onset of allergic conditions, the hygiene hypothesis has gained widespread acceptance [8]. This hypothesis states that the primary factor underlying increases in autoimmune diseases (including allergic conditions) is the decrease in infectious diseases due to improved hygiene and sanitation, and increased use of vaccines and antibiotics [9].

According to Gunawan et al. [23] the allergic potency of aeroallergens is linked to substances that have structural similarity to inflammatory lipid mediators including prostaglandin E_2 and leukotriene B_4. Lipid fractions from pollens promote chemotaxis and the activation of neutrophils and eosinophils. Additionally, allergenic pollens release proteases [75]. This proteolytic activity may also be involved in the development of allergic diseases. The combined actions of lipid mediators, proteases, and allergens in the respiratory system promote a disruption of normal cell barriers and a modification of antigen-presenting cells to exhibit predominately Th2 activity. In this microenvironment, the development of incident asthma is more likely [75].

In many children with asthma, the appearance of different allergic conditions follows a sequence that has been labelled the "atopic march" [76]. This sequence connects the different expressions of allergic diseases that vary with age, which often have transient symptoms. Typically, a large exposure to a potential allergen is followed by sensitization, according to the order in which infants are exposed to a predominant allergen: first food allergens (e.g., egg), then indoor allergens (e.g., dust mites), and finally, outdoor allergens (e.g., local anemopilous pollens) [69]. This sequence of exposures and sensitizations generally precedes the sequence of atopic symptoms that begins with food allergy and

associated gastrointestinal disorders, continues with atopic dermatitis, and progresses to respiratory allergies [77].

Because the first symptoms of the allergic conditions involved in the "atopic march" sometimes emerge during the first year of life, the first possible window for the environmental exposures responsible for these cases of atopy and asthma is likely to be open during gestation and the first months of life. This window is calculated considering two factors: (1) that only exposures preceding the first symptoms of an illness "can influence its inception" [67] (p. 2231); and (2) that antigens and air components can cross the placental barrier [78].

In other cases, such as pollen-related later-onset symptoms, allergies and asthma appear later in life when individuals are exposed to:

(a) new varieties of pollen through immigration to a new location [79,80] or through the appearance of botanical species in new geographical zones other than their native zones [81];
(b) higher than normal exposures to pollen, including in jobs that require long periods of contact with plants [82]. Occupational allergies and bronchial asthma have been reported in agricultural populations [83–85], florists [86], floriculturists [87], carpenters [88], and gardeners [89].

2.7. Variability in Sensitivity

A critical question for both pollen and fungi allergy is: how much aeroallergen exposure is needed for an allergic person need to develop sensitization and or exacerbation of existing disease? Most studies of exacerbation have found non-linear responses to indoor and outdoor allergens, indicating a threshold level for response [40,90,91]. In addition to a threshold for clinical symptoms, threshold exposure levels have also been described for the release of biological and inflammatory mediators [92]. The threshold values for fungi spores are generally higher than for pollen grains and range from $\geq$100 spores/m^3 for *Alternaria*, to $\geq$900 spores/m^3 for *Aspergillus/Penicillium*, to $\geq$3000 spores/m^3 for Cladosporium [93–96]. Although individuals vary widely in their reactivity to allergens, one proposed threshold for outdoor ragweed levels in the United States was estimated at 10 to 20 grains/m^3 for a period of at least 15 min [40]. During peak ragweed season, concentrations in North America can reach 250 grains/m^3, and they remain above 100 grains/m^3 for most of the season [97]. Likewise with tree pollen in Ontario, where mean in-season values of 300 grains/m^3 were recorded, with peaks reaching even higher [98]. Peaks reported for grass are somewhat lower, between 70 and 110 grains/m^3 to precipitate symptoms [99].

The priming effect is another important phenomenon involved in our understanding of the induction of allergic symptoms. The priming effect describes the transition from a state of minimal symptoms out of season to noticeable/bothersome symptoms after sufficient exposure to an allergen. It is formally defined as an increase in reactivity of the nasal membrane following repeated exposure [100]. Individuals who are already experiencing symptoms due to a perennial allergen (dust, pets, etc.) [101] or to high levels of air pollution [64] are more sensitive to subsequent exposure to aeroallergens. Conversely, when individuals with multiple sensitizations are 'primed' by an ongoing pollen season, they react more readily to allergens found in the home environment, such as dust [10,101]. The priming effect is relevant to consider when developing pollen warning or forecasting system in conjunction with existing systems for outdoor air pollutants. It demonstrates that those who suffer from seasonal allergies may have the ability to initiate short-term treatment such as antihistamines or sublingual immunotherapy within the first 3–5 days of the season to block the development of severe symptoms. However, those who are already suffering from poorly controlled allergic rhinitis or asthma are in danger of reacting severely and almost immediately upon the arrival of pollen season due to pre-priming [102].

2.8. Development of Respiratory Allergies: Risk/Protective Factors

The most promising mechanism that can explain the development of allergies involves interactions between individual genetic susceptibility and environmental exposures [103]. For example,

gene–environment interactions have been demonstrated with changes in microRNA [3] and bronchial epithelial DNA methylation, after exposures to diesel exhaust [104]. For individuals with atopy-prone or immune modulated genotypes, environmental exposures play a role in the onset of an allergic disorder [105], including exposures to aeroallergens [2,106]. However, the environmental effect may be either detrimental or protective; Tovey et al. [91] found a non-linear relationship between mite allergen exposure and sensitization and asthma, with children on the lowest and highest quintile of exposure less likely to have both sensitization and asthma compared with the middle range of exposures.

2.9. Protective Factors

An environmental exposure can be considered as a protective factor if it is linked to decreased risk of the development of a specific condition [105].

2.9.1. Animals

An increasing number of studies indicate that exposure to domestic animals (pets or livestock) in early life decreases the risk of asthma [67], aeroallergen sensitization [107], and respiratory allergic disease as a whole [108]. The immune system modulation caused by these exposures is aligned with the hygiene hypothesis in which microbial exposures shift the immune response towards Th1 predominance [8,109,110].

Early and prolonged contact with animals [111] seems to have a protective effect against sensitization to aeroallergens, particularly if the exposure happens during the two first years of life [107]. The benefit appears to continue throughout the life course [112]. Exposures to farm animals seem to reduce specific aeroallergen IgE antibody production [113], particularly with higher exposures [114].

2.9.2. Breastfeeding

Breastfeeding, defined as the consumption of human breast milk through infant suckling directly from the breast, is acknowledged as an optimal source of infant nutrition [115]. Despite the short-term clinical and societal benefits, evidence has been mixed on the role of breastfeeding in the development of atopic conditions.

Breastfeeding has been associated with decreased risk of child atopy and the different phenotypes of asthma [116]. Although some factors such as maternal atopy might confound this association [117], reduced risk is present mostly with exclusive breastfeeding when compared with consumption of expressed milk or combined breast milk and formula [115]. Risk reduction extends well into school age, but is most pronounced in children 0–2 years [116].

2.10. Risk Factors

To consider an environmental element as a risk factor, it is necessary to demonstrate a positive exposure–response relationship with the allergic outcome of interest [103]. Interactions between pollen and the following environmental conditions have been studied and linked to increased risk for the development of an allergic condition [118].

2.10.1. Weather

In northern climates such as Canada, pollen production, dispersal, and airborne lifespan are highly dependent on the weather. In general, trees bloom in the early spring, grasses bloom late spring to early summer, and weeds pollinate in the fall [40]. Ragweed is in late August until the first frost, and thus ragweed season can be cut short by an early frost [32,119]. The weather in the current year has less effect on the intensity of the tree pollen season than the weather in the previous year, because trees produce pollen in the summer and fall, then release it when a sufficient number of warm days occur in

the following spring [32,119]. Thus, the amount of tree pollen released depends on the weather in the previous year, but the timing of release depends on the current spring weather [32].

Diurnal changes in pollen levels have also been observed. As ragweed pollen is released in the morning, peak concentrations are reached around noon in the absence of high winds or rain [120]. Depending on the temperature, humidity, and wind conditions, the counts may drop at night or remain elevated [40,121]. Mature pollen grains tend to be released when the relative humidity drops, and they remain airborne longer at low humidity, low wind speeds, and high atmospheric pressure [120]. Meteorological conditions also affect fungi sporulation, as many grow well when conditions are wet and they produce spores as a survival mechanism when conditions are dry [40,121].

Precipitation can temporarily clear particles and aeroallergens from the air, although some pollen grains or fungi spores may be resuspended after a brief rainfall [36,122]. Exposure to water may also increase the formation of both pollen and fungi aeroallergens in a 24-h timeframe [40]. Considering the added complexity of rainfall, it is possible that the presence of high counts may be sufficient, but not necessary, for significant aeroallergen exposure to occur, due to the ruptured aeroallergen grains that are not accurately counted during these events [40].

Thunderstorms can be associated with asthma exacerbations, with steep increases in the use of emergency services and increased mortality [123–125]. Thunderstorms during pollen season are known to carry whole and ruptured pollen grains at the ground level where wind outflows distribute them with larger geographic coverage than under normal conditions [126]. Climate change has been linked to an increase in frequency of thunderstorms in some areas [127].

2.10.2. Seasonality

The division of the year into four seasons (spring, summer, fall, and winter) takes into consideration variables that undergo yearly cyclical changes, such as day length, temperature, and humidity. The influence of these factors on aeroallergens can be direct and indirect [128], and all have been associated with allergic respiratory morbidity [129–131] and mortality [132,133]. There is some indication of an association between season of birth on the development of asthma and allergies [134]. If an individual is exposed to high aeroallergen counts in utero and/or during the sensitive immune system development period of the first months of life, there may be at risk of atopic disease later in life [135–137].

2.10.3. Urbanization

Living in urban areas, as opposed to rural and semi-rural areas, is a known risk factor for the development of aeroallergen-induced respiratory allergy [128,138]. There is evidence that highly allergenic species of fungi are present at higher levels in the outdoor air in cities compared with rural environments [139]. Differences between aeroallergen counts (higher in the rural areas) and species diversity (lower in urban areas) may drive some of the differences between rural and urban influence on the onset of allergies and asthma [140]. Additionally, the higher levels of air pollutants predominant in urban areas can interact with airborne pollen grains, which is likely to exacerbate allergic conditions and respiratory distress [128]. Two thirds of the global population will live in urban areas by 2020, and an increased risk for aeroallergen-induced respiratory allergy is expected [127].

2.10.4. Air Pollution

The interactions between air pollution and aeroallergens are complex and occur both in the atmosphere and in the airways [141]. Ziska et al. [142] have demonstrated that outdoor air pollution can prompt an increase in pollen production by certain herbaceous species, similar to the effects seen with increased CO_2. A number of studies have also shown that air pollution may increase the allergenicity of pollen and/or fungi, because air pollutants can attach to the surface of pollen grains and potentially alter their allergenic potential and morphology by making the surface of the pollen grain coating more fragile [128,143,144]. Timing of exposure is important, and co-occurence of

pollen/spore release and increased air pollution episodes appears to be the most harmful in terms of increased allergenicity. Ragweed pollen is released from early to mid-morning, peaking around noon [145]. Air pollution monitoring data from various cities has shown that traffic-related air pollution (TRAP) follows a diurnal pattern with an increase during the daily rush hours [146–148]. Air pollution in combination with sunlight can lead to the photochemical production of ground-level ozone, which typically peaks in the afternoon. Thus, the diurnal patterns of pollen release, TRAP, and ozone concentrations in cities may place high levels of aeroallergens in contact with relatively high daily levels of air pollution, potentially leading to ambient modifications of the allergenicity of aeroallergens [146].

In the airway, oxidative stress has been identified as a major biologic pathway for the effects of most of the air pollutants components (e.g., $PM_{2.5}$, ground-level ozone, nitrogen dioxide (NO_2) and sulfur dioxide (SO_2) [149,150]. Air pollutants allow for easier penetration of pollen and spore allergens because they trigger damage to the airway mucociliary clearance mechanisms [128,141]. Particulate matter smaller than 2.5 µm ($PM_{2.5}$) reaches deeply in the lungs and acts as an adjuvant that increases production of IgE [3,151,152]. Furthermore, exposure to diesel exhaust is known to impact DNA methylation and impaired regulatory T-cell functions, two mechanisms relevant for the immune response [104]. Changes in FEV1 following allergen exposure have also been modified by controlled diesel exhaust exposure and *GST* genotype in a gene–environment interaction manner [152]. These GST variants are commonly present in the general population (i.e., from 23% to 62% depending on the ethnic group, in the USA) [153], so many people might experience amplified effects of air pollution–aeroallergen co-exposures in the outdoor environment.

2.11. Fundamentals of the Allergic Response

In humans, immune responses can range from diminished (i.e., immunosuppression) to heightened (i.e., allergies) [72], with a biologically appropriate response in the middle of these extremes (i.e., appropriate recognition and response to harmful pathogens) [55]. Pollen grains carry cytoplasmic granules that release a number of proteins and glycoproteins when they are exposed to water or airborne pollutants. These proteins instigate the adverse immune response in sensitized individuals (Figure 3) [128,154–156]. In addition, single and repeated exposures to pollen in allergic individuals have been shown to induce epigenetic changes, both in the blood and the nasal tissue [157].

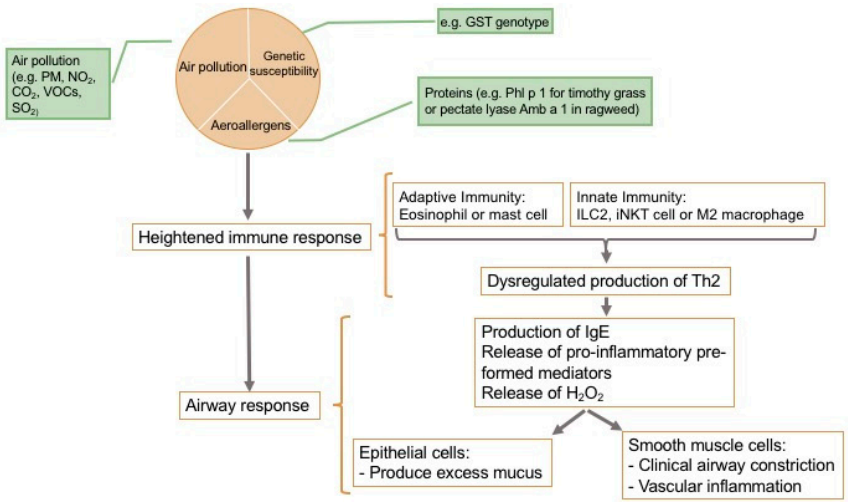

Figure 3. Adverse immune response in the airway, adapted from [158].

The impact of aeroallergens has been documented in every section of the airway. The nose is the first point of contact with aeroallergens, and the histamine released due to interaction with aeroallergens increases tissue swelling and permeability, causing rhinitis and rhinorrhea [59]. Rhinitis

is a risk factor for the development of asthma [60] and allergic rhinitis is most commonly due to pollen allergy [159].

Due to the many similarities between the nasal and bronchial mucosa and their reactions to aeroallergens, the "one airway, one disease" concept has been proposed for allergic rhinitis and allergic asthma [160]. Approximately 80% of patients with allergic asthma also have allergic rhinitis symptoms upon exposure to aeroallergens, but not all people with allergic rhinitis experience asthma symptoms [160–162]. Sensitization to aeroallergens is a major contributing factor to this discrepancy [163].

The hyper-responsiveness of the airways and subsequent constriction following allergen exposure are distinctive clinical findings in asthma [103,164,165]. Constriction is due to inflammatory processes and airway remodeling. Reversibility of the inflammation over time or by medication are also considered in asthma diagnosis [74]. Wheeze, cough, and paroxysmal dyspnea are less specific clinical signs of asthma. Persistent symptoms, triggered by the Th2 and IgE interactions, lead to structural changes and remodeling of the airway [166].

Asthma is a complex disease that can be understood as a syndrome, because different pathways can result in diverse phenotypes [74]. Several clinical phenotypes of asthma display differences in severity, inflammatory pattern, and comorbidity with allergic diseases (since not all asthma is atopic) [167]. Reversible bronchoconstriction, either spontaneously or after bronchodilator treatment, remains a common process in all the phenotypes [166].

Among respiratory conditions, asthma is one of the major non-communicable chronic diseases. Globally, approximately 235 million people currently suffer from asthma [168]. In high-income countries such as Canada, prevalence rose for many years from the early 1960s to 2000 [19,128] and recently seems to have reached a plateau [126,169].

2.12. Prevalence of Respiratory Allergies in Canada

Allergic rhinitis is highly prevalent in Canada, affecting approximately 20–25% of the population [170]. Asthma is estimated to affect about 3 million Canadians, and between 12% [171] to 25% of Canadian children [172–174]. Approximately two-thirds of people with asthma are allergic to aeroallergens, and these allergens act as triggers for asthma exacerbations [15]. Overall, approximately 7.7 million were people affected by aeroallergens in Canada in 2016 (Figure 4) [175]. High concentrations of ambient aeroallergens, including tree pollen, fungal spores, and others, have been associated with increased risk of early delivery [176], myocardial infarction [98], as well as with asthma-related emergency department visits and hospitalizations in cities across Canada, demonstrating that severe symptoms are related to aeroallergen counts across the country [177–181].

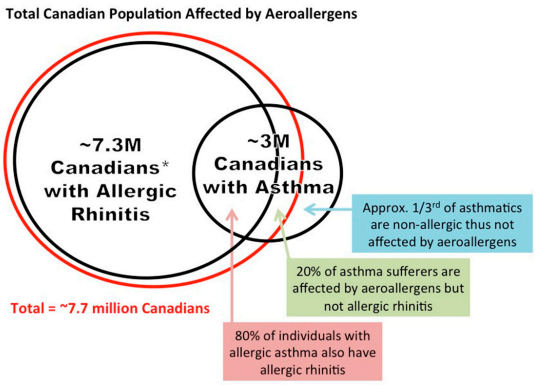

Figure 4. Total Canadian population affected by aeroallergens. This estimation of the total allergic population is based on the conservative estimate that 20% of the Canadian population is affected by allergic rhinitis, and the total population of Canada used in this calculation was based on 2016 data from Statistics Canada [175].

2.13. Economic Costs Associated with Respiratory Allergies

Atopic conditions represent a large burden on the economy. A study in British Columbia found that excess costs to the healthcare system in patients with asthma were $1028.00 per patient/year, compared with a control group [182]. This included the direct costs of asthma, as well as publicly-funded healthcare costs related to comorbid conditions in people with asthma, including allergic rhinitis [182]. Asthma is also the leading driver of health care costs for children in Canada, estimated at over $2 billion per year [183]. Recent estimates suggest that in a single year (between 2014–2015), asthma attacks triggered over 70,000 emergency room visits [184]. The costs of asthma to the Canadian economy are also expected to rise to almost $4 billion per year by 2030, more than double the current cost [185].

2.14. Effects of Climate Change on Aeroallergens

Levels of some specific aeroallergens are on the rise in particular regions, and some of this increase has been linked to anthropogenic climate change [186]. Anthropogenic climate change has been documented over the past 100 years and is projected to continue to intensify [81], driven in part by increases in temperature [138,187]. As seen on Figure 5, the increasing planetary temperatures affect plant biology through the timing and length of the growing seasons [188], increased production and allergenicity of pollen, and shifts in range of species [186,189].

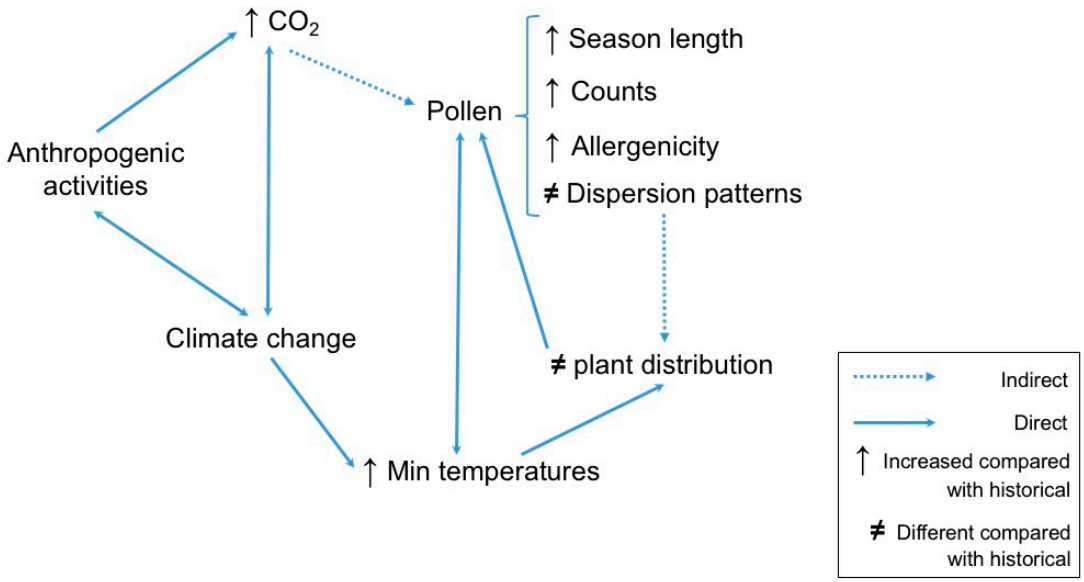

Figure 5. Effects of climate change on aeroallergens.

Due to the warmer temperatures, pollen seasons will start earlier and end later [66,138,155,190]. Warming by latitude has been associated with increased length of the ragweed pollen season in North America, increasing by 27 days between 1995 and 2009 [149]. Earlier seasonal starts have also been found for *Juniperus*, *Ulmus*, and *Morus* [81]. In Western Europe, spring events have advanced by six days [191] and changes in birch pollen season [192] and *Artemisia* have been described [193]. Changes in length will lead to changes in human exposure [194] and potentially in sensitization [2,189].

Increased pollen counts have been associated with the current levels of CO_2, when compared with CO_2 levels of the previous century [195] or even between different decades (2004 and 2013 in Ariano et al.) [186,196]. Increases in the atmospheric concentrations of CO_2 impact the reproductive processes in plants, leading them to produce more pollen [111,197,198] with significantly stronger allergenicity has been found in pollen [81,193,199]. This increased allergenicity is due to more diversity in the heterogeneity of the antigenic proteins in pollen grains [62].

Climate change affects many meteorological variables that participate in the pollen dispersal and deposition (i.e., humidity, precipitation, and temperature) [127]. Changes in dispersion, both region- and species-specific, can potentially expose (and sensitize) populations to novel allergens [141]. These changes in dispersion will also impact plant distribution, as species that could not survive in previously hostile environments can potentially thrive because of changes in temperature and precipitation [193]. The proliferation of anemophilous plants where those species were not previously prevalent exposes atopy-prone individuals to new pollens [200].

2.15. Environment and Health Interventions for Patients with Respiratory Allergies

Allergic asthma is managed through allergen avoidance and pharmacotherapy to achieve and maintain asthma control [201].

The Canadian guidelines state that, after their diagnoses, patients and/or caregivers should receive a written asthma action plan and self-management education [201]. Pharmacotherapy should be part of the written asthma plan and is designed to be long-term to prevent exacerbations. Thus, aside from the self-administration of short-acting beta-agonists as needed, pharmacotherapy for asthma is not typically altered based on current aeroallergen levels except to ensure that such long-term controller medications are used properly and as prescribed. For those who are allergic to seasonal aeroallergens, knowledge of current or upcoming pollen or fungi counts may aid in both avoidance and the optimization of pharmacotherapy [127]. If certain aeroallergens are known to exacerbate individual asthma symptoms, allergen avoidance is one option (although it may not always be feasible), and immunotherapy may be recommended in advance of the allergy season. Most people with allergic asthma also have allergic rhinitis, and the treatment of both disorders during times of increased aeroallergen presence has been shown to be critical to the maintenance of asthma control; therefore, supporting the optimization of allergic rhinitis therapy by providing information on aeroallergen levels may have a profound impact on many patients with allergic asthma [162].

The efficacies of most prescribed medications for allergic rhinitis are enhanced if they are taken consistently and/or before symptom onset [170]. Thus, reminders and warnings that various aeroallergen seasons, wildfire exposures, elevated air pollution episodes or thunderstorms are approaching may allow Canadians to ensure they have visited a healthcare provider, refilled prescriptions, and begun taking preventative medications according to their management plan [202].

3. Conclusions

Pollen and fungi are important allergen in the outdoor air [57]. Aeroallergens play a critical role in the development of allergic conditions through sensitization, particularly in those individuals with genetic predisposition [203].

Pollen and fungi do not act in isolation. Other environmental exposures (e.g., TRAP) also play a role in the interaction between air and respiratory tissue [103]. Environmental exposures can act as risk or protective factors in the development of allergy to aeroallergens [204]. After the sensitization takes place and the affected individual develops symptoms, further exposures to risk factors may cause symptom exacerbations that will diminish with reduced exposure or with medical treatment [67].

An aeroallergen alert system could be used to communicate with sensitized individuals and advise them to control their exposure when aeroallergen counts are high. An aeroallergen alert system would benefit from a model of aeroallergen production and dispersion that also incorporates weather-related variations and long-term impacts of climate change and could be coupled with existing air quality predictions. Given the documented clinical cross-reactivity between pollens from similar species [30], the idea of reporting total tree, grass, and ragweed pollens is better suited to the general public for simplicity and cost minimization, while counts of individual species would still have value for modeling and research.

Climate change has the potential to increase the length of aeroallergen seasons as well as pollen counts, geographical coverage, and allergenicity [19]. These increases will also increase human

exposure to the allergenic proteins found in pollen grains [155,193]. Future increases in the incidence and prevalence of respiratory allergies and asthma are predicted [194], accompanied by an increase in health care expenses allotted to the care of these conditions [62]. Longitudinal studies are needed to examine long-term trends beyond the yearly variations due to variation in aeroallergen seasons. Such studies would help explain regional differences in risk and increase our understanding of the impact of climate change on pollens and fungi [18].

Better understanding of both pollen and fungi counts, phenology, geographic coverage, and interaction with air pollutants is needed to provide the information that atopic individuals could use to modify their environmental exposures [127], and also to shape government initiatives such as alert systems and landscaping in urban zones [205].

Supplementary Materials: The following is available online at http://www.mdpi.com/1660-4601/15/8/1577/s1, Table S1: Plant-Derived Aeroallergens in the Major Floristic Zones of Canada.

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References

1. Lau, S. Are asthma and allergies increasing in children and adolescents? *Eur. J. Integr. Med.* **2009**, *1*, 175. [CrossRef]
2. Breton, M.-C.; Garneau, M.; Fortier, I.; Guay, F.; Louis, J. Relationship between climate, pollen concentrations of Ambrosia and medical consultations for allergic rhinitis in Montreal, 1994–2002. *Sci. Total Environ.* **2006**, *370*, 39–50. [CrossRef] [PubMed]
3. Rider, C.F.; Yamamoto, M.; Günther, O.P.; Hirota, J.A.; Singh, A.; Tebbutt, S.J.; Carlsten, C. Controlled diesel exhaust and allergen coexposure modulates microRNA and gene expression in humans: Effects on inflammatory lung markers. *J. Allergy Clin. Immunol.* **2016**, *138*, 1690–1700. [CrossRef] [PubMed]
4. Smits, H.H.; van der Vlugt, L.E.; von Mutius, E.; Hiemstra, P.S. Childhood allergies and asthma: New insights on environmental exposures and local immunity at the lung barrier. *Curr. Opin. Immunol.* **2016**, *42*, 41–47. [CrossRef] [PubMed]
5. Cardaba, B.; Llanes, E.; Chacartegui, M.; Sastre, B.; Lopez, E.; Molla, R.; Del Pozo, V.; Florido, F.; Quiralte, J.; Palomino, P.; et al. Modulation of allergic response by gene-environment interaction: Olive pollen allergy. *J. Investig. Allergol. Clin. Immunol.* **2007**, *17* (Suppl. 1), 31–35. [PubMed]
6. Huang, F.; Yin, J.-N.; Wang, H.-B.; Liu, S.-Y.; Li, Y.-N. Association of imbalance of effector T cells and regulatory cells with the severity of asthma and allergic rhinitis in children. *Allergy Asthma Proc.* **2017**, *38*, 70–77. [CrossRef] [PubMed]
7. Sun, R.; Tang, X.-Y.; Yang, Y. Immune imbalance of regulatory T/type 2 helper cells in the pathogenesis of allergic rhinitis in children. *J. Laryngol. Otol.* **2016**, *130*, 89–94. [CrossRef] [PubMed]
8. Sears, M.R.; Greene, J.M.; Willan, A.R.; Taylor, D.R.; Flannery, E.M.; Cowan, J.O.; Herbison, G.P.; Poulton, R. Long-term relation between breastfeeding and development of atopy and asthma in children and young adults: A longitudinal study. *Lancet* **2002**, *360*, 901–907. [CrossRef]
9. Bach, J.-F. The Effect of Infections on Susceptibility to Autoimmune and Allergic Diseases. *N. Engl. J. Med.* **2002**, *347*, 911–920. [CrossRef] [PubMed]
10. Ellis, A.K.; Ratz, J.D.; Day, A.G.; Day, J.H. Factors that affect the allergic rhinitis response to ragweed allergen exposure. *Ann. Allergy Asthma Immunol.* **2010**, *104*, 293–298. [CrossRef] [PubMed]

11. Patel, D.; Lee, J.S.; Wilson, D.; Camuso, N.; Salapatek, A. Repeated Low-dose Aerosolized Dust Mite Allergen Exposure in Asthmatic and Non-asthmatic Dust Mite Allergic patients in An Environmental Exposure Chamber Induces Specific Asthma Symptoms as well as Allergic Rhinoconjunctivitis Symptoms. *J. Allergy Clin. Immunol.* **2011**, *127*, AB20. [CrossRef]
12. Rondón, C.; Fernández, J.; López, S.; Campo, P.; Doña, I.; Torres, M.J.; Mayorga, C.; Blanca, M. Nasal inflammatory mediators and specific IgE production after nasal challenge with grass pollen in local allergic rhinitis. *J. Allergy Clin. Immunol.* **2009**, *124*, 1005–1011. [CrossRef] [PubMed]
13. Gieras, A.; Focke-Tejkl, M.; Ball, T.; Verdino, P.; Hartl, A.; Thalhamer, J.; Valenta, R. Molecular determinants of allergen-induced effector cell degranulation. *J. Allergy Clin. Immunol.* **2007**, *119*, 384–390. [CrossRef] [PubMed]
14. Weber, R.W. Floristic zones and aeroallergen diversity. *Immunol. Allergy Clin. N. Am.* **2003**, *23*, 357–369. [CrossRef]
15. Lafeuille, M.-H.; Gravel, J.; Figliomeni, M.; Zhang, J.; Lefebvre, P. Burden of illness of patients with allergic asthma versus non-allergic asthma. *J. Asthma* **2013**, *50*, 900–907. [CrossRef] [PubMed]
16. Grant-Downton, R.; Hafidh, S.; Twell, D.; Dickinson, H.G. Small RNA Pathways Are Present and Functional in the Angiosperm Male Gametophyte. *Mol. Plant* **2009**, *2*, 500–512. [CrossRef] [PubMed]
17. Farré-Armengol, G.; Filella, I.; Llusià, J.; Peñuelas, J. Pollination mode determines floral scent. *Biochem. Syst. Ecol.* **2015**, *61*, 44–53. [CrossRef]
18. Park, H.J.; Lee, J.-H.; Park, K.H.; Kim, K.R.; Han, M.J.; Choe, H.; Oh, J.W.; Hong, C.S. A Six-Year Study on the Changes in Airborne Pollen Counts and Skin Positivity Rates in Korea: 2008–2013. *Yonsei Med. J.* **2016**, *57*, 714–720. [CrossRef] [PubMed]
19. D'Amato, G.; Vitale, C.; De Martino, A.; Viegi, G.; Lanza, M.; Molino, A.; Sanduzzi, A.; Vatrella, A.; Annesi-Maesano, I.; D'amato, M. Effects on asthma and respiratory allergy of Climate change and air pollution. *Multidiscip. Respir. Med.* **2015**, *10*, 39. [CrossRef] [PubMed]
20. Katelaris, C.H.; Beggs, P.J. Climate change: Allergens and allergic diseases. *Intern. Med. J.* **2018**, *48*, 129–134. [CrossRef] [PubMed]
21. Lacey, J. Spore dispersal—Its role in ecology and disease: The British contribution to fungal aerobiology. *Mycol. Res.* **1996**, *100*, 641–660. [CrossRef]
22. Pablos, I.; Wildner, S.; Asam, C.; Wallner, M.; Gadermaier, G. Pollen Allergens for Molecular Diagnosis. *Curr. Allergy Asthma Rep.* **2016**, *16*, 31. [CrossRef] [PubMed]
23. Gunawan, H.; Takai, T.; Kamijo, S.; Wang, X.L.; Ikeda, S.; Okumura, K.; Ogawa, H. Characterization of proteases, proteins, and eicosanoid-like substances in soluble extracts from allergenic pollen grains. *Int. Arch. Allergy Immunol.* **2008**, *147*, 276–288. [CrossRef] [PubMed]
24. Skjøth, C.A.; Šikoparija, B.; Jäger, S. EAN-Network. Pollen Sources. In *Allergenic Pollen*; Springer: Dordrecht, The Netherlands, 2013; pp. 9–27. Available online: http://link.springer.com/chapter/10.1007/978-94-007-4881-1_2 (accessed on 31 May 2018).
25. Ellis, A.K.; Soliman, M.; Steacy, L.; Boulay, M.-È.; Boulet, L.-P.; Keith, P.K.; Vliagoftis, H.; Waserman, S.; Neighbour, H. The Allergic Rhinitis–Clinical Investigator Collaborative (AR-CIC): Nasal allergen challenge protocol optimization for studying AR pathophysiology and evaluating novel therapies. *Allergy Asthma Clin. Immunol.* **2015**, *11*, 16. [CrossRef] [PubMed]
26. Ellis, A.K.; North, M.L.; Walker, T.; Steacy, L.M. Environmental exposure unit: A sensitive, specific, and reproducible methodology for allergen challenge. *Ann. Allergy Asthma Immunol.* **2013**, *111*, 323–328. [CrossRef] [PubMed]
27. White, J.F.; Bernstein, D.I. Key pollen allergens in North America. *Ann. Allergy Asthma Immunol.* **2003**, *91*, 425–435. [CrossRef]
28. Léonard, R.; Wopfner, N.; Pabst, M.; Stadlmann, J.; Petersen, B.O.; Duus, J.Ø.; Himly, M.; Radauer, C.; Gadermaier, G.; Razzazzi-Fazeli, E.; et al. A new allergen from ragweed (*Ambrosia artemisiifolia*) with homology to art v 1 from mugwort. *J. Biol. Chem.* **2010**, *285*, 27192. [CrossRef] [PubMed]
29. Oberhuber, C.; Ma, Y.; Wopfner, N.; Gadermaier, G.; Dedic, A.; Niggemann, B.; Maderegger, B.; Gruber, P.; Ferreira, F.; Scheiner, O.; et al. Prevalence of IgE-Binding to Art v 1, Art v 4 and Amb a 1 in Mugwort-Allergic Patients. *Int. Arch. Allergy Immunol.* **2008**, *145*, 94–101. [CrossRef] [PubMed]
30. Asero, R.; Wopfner, N.; Gruber, P.; Gadermaier, G.; Ferreira, F. Artemisia and Ambrosia hypersensitivity: Co-sensitization or co-recognition? *Clin. Exp. Allergy* **2006**, *36*, 658–665. [CrossRef] [PubMed]

31. Eriksson, N.E.; Wihl, J.A.; Arrendal, H.; Strandhede, S.O. Tree pollen allergy. II. Sensitization to various tree pollen allergens in Sweden. A multi-centre study. *Allergy* **1984**, *39*, 610–617. [CrossRef] [PubMed]
32. Sutherland, S. News—Pollen Season Is upon US. Who's Getting it Bad This Year? The Weather Network. Available online: https://www.theweathernetwork.com/news/articles/pollen-season-is-upon-us-whos-getting-it-bad-this-year/66940 (accessed on 31 May 2018).
33. Weinberger, K.R.; Kinney, P.L.; Robinson, G.S.; Sheehan, D.; Kheirbek, I.; Matte, T.D.; Lovasi, G.S. Levels and determinants of tree pollen in New York City. *J. Expo. Sci. Environ. Epidemiol.* **2018**, *28*, 119–124. [CrossRef] [PubMed]
34. Hugg, T.T.; Hjort, J.; Antikainen, H.; Rusanen, J.; Tuokila, M.; Korkonen, S.; Weckström, J.; Jaakkola, M.S.; Jaakkola, J.J. Urbanity as a determinant of exposure to grass pollen in Helsinki Metropolitan area, Finland. *PLoS ONE* **2017**, *12*, e0186348. [CrossRef] [PubMed]
35. Rogers, C.A. An aeropalynological study of metropolitan Toronto. *Aerobiologia* **1997**, *13*, 243–257. [CrossRef]
36. Solomon, W.R. Airborne pollen: A brief life. *J. Allergy Clin. Immunol.* **2002**, *109*, 895–900. [CrossRef] [PubMed]
37. Agarwal, M.K.; Swanson, M.C.; Reed, C.E.; Yunginger, J.W. Immunochemical quantitation of airborne short ragweed, Alternaria, antigen, E.; and Alt-I allergens: A two-year prospective study. *J. Allergy Clin. Immunol.* **1983**, *72*, 40–45. [CrossRef]
38. Agarwal, M.K.; Swanson, M.C.; Reed, C.E.; Yunginger, J.W. Airborne ragweed allergens: Association with various particle sizes and short ragweed plant parts. *J. Allergy Clin. Immunol.* **1984**, *74*, 687–693. [CrossRef]
39. Grote, M.; Vrtala, S.; Niederberger, V.; Wiermann, R.; Valenta, R.; Reichelt, R. Release of allergen-bearing cytoplasm from hydrated pollen: A mechanism common to a variety of grass (Poaceae) species revealed by electron microscopy. *J. Allergy Clin. Immunol.* **2001**, *108*, 109–115. [CrossRef] [PubMed]
40. Portnoy, J.; Barnes, C. Clinical relevance of spore and pollen counts. *Immunol. Allergy Clin. N. Am.* **2003**, *23*, 389–410. [CrossRef]
41. Levetin, E.; Horner, W.E.; Scott, J.A. Taxonomy of Allergenic Fungi. *J. Allergy Clin. Immunol. Pract.* **2016**, *4*, 375–385. [CrossRef] [PubMed]
42. Hibbett, D.S.; Binder, M.; Bischoff, J.F.; Blackwell, M.; Cannon, P.F.; Eriksson, O.E.; Huhndorf, S.; James, T.; Kirk, P.M.; Lücking, R.; et al. A higher-level phylogenetic classification of the Fungi. *Mycol. Res.* **2007**, *111*, 509–547. [CrossRef] [PubMed]
43. McLaughlin, D.J.; Hibbett, D.S.; Lutzoni, F.; Spatafora, J.W.; Vilgalys, R. The search for the fungal tree of life. *Trends Microbiol.* **2009**, *17*, 488–497. [CrossRef] [PubMed]
44. Aukrust, L. Mold allergy. Introduction. *Clin. Rev. Allergy* **1992**, *10*, 147–151. [PubMed]
45. Burge, H.A. Classification of the fungi. *Clin. Rev. Allergy* **1992**, *10*, 153–163. [PubMed]
46. Taylor, J.; Jacobson, D.; Fisher, M. The Evolution of Asexual Fungi: Reproduction, Speciation and Classification. *Annu. Rev. Phytopathol.* **1999**, *37*, 197–246. [CrossRef] [PubMed]
47. Crameri, R.; Zeller, S.; Glaser, A.G.; Vilhelmsson, M.; Rhyner, C. Cross-reactivity among fungal allergens: A clinically relevant phenomenon? *Mycoses* **2009**, *52*, 99–106. [CrossRef] [PubMed]
48. Singh, A.B. Pollen and Fungal Aeroallergens Associated with Allergy and Asthma in India. *Glob. J. Immunol. Allerg. Dis.* **2014**, *2*, 19–28. [CrossRef]
49. Akiyama, K. The role of fungal allergy in bronchial asthma. *Nihon Ishinkin Gakkai Zasshi Jpn. J. Med. Mycol.* **2000**, *41*, 149–155. [CrossRef]
50. Weber, R.W. Outdoor aeroallergen sampling: Not all that simple. *Ann. Allergy Asthma Immunol.* **2007**, *98*, 505–506. [CrossRef]
51. Weber, R.W. Pollen Identification. *Ann. Allergy Asthma Immunol.* **1998**, *80*, 141–148. [CrossRef]
52. Crouzy, B.; Stella, M.; Konzelmann, T.; Calpini, B.; Clot, B. All-Optical automatic pollen identification: Towards an operational system. *Atmos. Environ.* **2016**, *140*, 202–212. [CrossRef]
53. Levetin, E.; Van de Water, P.K. Pollen count forecasting. *Immunol. Allergy Clin. N. Am.* **2003**, *23*, 423–442. [CrossRef]
54. Hjort, J.; Hugg, T.T.; Antikainen, H.; Rusanen, J.; Sofiev, M.; Kukkonen, J.; Jaakkola, M.S.; Jaakkola, J.J. Fine-Scale Exposure to Allergenic Pollen in the Urban Environment: Evaluation of Land Use Regression Approach. *Environ. Health Perspect.* **2016**, *124*, 619–626. [CrossRef] [PubMed]

55. Esser, C. Principles of the Immune System: Players and Organization. In *Environmental Influences on the Immune System*; Springer: Vienna, Austria, 2016; pp. 1–17. Available online: http://link.springer.com/chapter/10.1007/978-3-7091-1890-0_1 (accessed on 31 May 2018).
56. Graham-Rowe, D. Lifestyle: When allergies go west. *Nature* **2011**, *479*, S2–S4. [CrossRef]
57. Cecchi, L. Introduction. In *Allergenic Pollen*; Springer: Dordrecht, The Netherlands, 2013; pp. 1–7. Available online: http://link.springer.com/chapter/10.1007/978-94-007-4881-1_1 (accessed on 31 May 2018).
58. De Weger, L.A.; Bergmann, K.C.; Rantio-Lehtimäki, A.; Dahl, Å.; Buters, J.; Déchamp, C.; Belmonte, J.; Thibaudon, M.; Cecchi, L.; Besancenot, J.P.; et al. Impact of Pollen. In *Allergenic Pollen*; Sofiev, M., Bergmann, K.-C., Eds.; Springer: Dordrecht, The Netherlands, 2013; pp. 161–215. Available online: http://link.springer.com/10.1007/978-94-007-4881-1_6 (accessed on 31 May 2018).
59. Cantani, A. Allergic Rhinitis. In *Pediatric Allergy, Asthma and Immunology*; Springer: Berlin, Germany, 2008; pp. 875–910. Available online: http://link.springer.com.proxy.lib.sfu.ca/chapter/10.1007/978-3-540-33395-1_12 (accessed on 18 July 2016).
60. Vaitla, P.M.; Drewe, E. Identifying the culprit allergen in seasonal allergic rhinitis. *Practitioner* **2011**, *255*, 27–31. [PubMed]
61. Hesse, M.; Halbritter, H.; Zetter, R.; Weber, M.; Buchner, R.; Frosch-Radivo, A.; Ulrich, S.; Zetter, R. Pollen Morphology. In *Pollen Terminology an Illustrated Handbook*; Springer: Wien, Austria, 2009.
62. Szema, A.M. Asthma, Hay Fever, Pollen, and Climate Change. In *Global Climate Change and Public Health*; Pinkerton, K.E., Rom, W.N., Eds.; Springer: New York, NY, USA, 2014; pp. 155–165. Available online: http://link.springer.com.proxy.lib.sfu.ca/chapter/10.1007/978-1-4614-8417-2_9 (accessed on 15 July 2016).
63. Green, B.J.; Beezhold, D.H.; Gallinger, Z.; Barron, C.S.; Melvin, R.; Bledsoe, T.A.; Kashon, M.L.; Sussman, G.L. Allergic sensitization in Canadian chronic rhinosinusitis patients. *Allergy Asthma Clin. Immunol.* **2014**, *10*, 15. [CrossRef] [PubMed]
64. Cakmak, S.; Dales, R.E.; Coates, F. Does air pollution increase the effect of aeroallergens on hospitalization for asthma? *J. Allergy Clin. Immunol.* **2011**, *129*, 228–231. [CrossRef] [PubMed]
65. Sandin, A.; Bjorksten, B.; Braback, L. Development of atopy and wheezing symptoms in relation to heredity and early pet keeping in a Swedish birth cohort. *Pediatr. Allergy Immunol.* **2004**, *15*, 316–322. [CrossRef] [PubMed]
66. D'Amato, G.; Vitale, C.; Lanza, M.; Molino, A.; D'Amato, M. Climate change, air pollution, and allergic respiratory diseases: An update. *Curr. Opin. Allergy Clin. Immunol.* **2016**, *16*, 434–440. [CrossRef] [PubMed]
67. Eder, W.; Ege, M.J.; von Mutius, E. The Asthma Epidemic. *N. Engl. J. Med.* **2006**, *355*, 2226–2235. [CrossRef] [PubMed]
68. Armentia, A.; Banuelos, C.; Arranz, M.L.; Del Villar, V.; Martin-Santos, J.M.; Gil, F.J.; Gil, F.M.; Vega, J.M.; Callejo, A.; Paredes, C. Early introduction of cereals into children's diets as a risk-factor for grass pollen asthma. *Clin. Exp. Allergy* **2001**, *31*, 1250–1255. [CrossRef] [PubMed]
69. Halken, S. Prevention of allergic disease in childhood: Clinical and epidemiological aspects of primary and secondary allergy prevention. *Pediatr. Allergy Immunol.* **2004**, *15*, 9–32. [CrossRef] [PubMed]
70. Bardei, F.; Bouziane, H.; Kadiri, M.; Rkiek, B.; Tebay, A.; Saoud, A. Skin sensitisation profiles to inhalant allergens for patients in Tetouan city (North West of Morocco). *Rev. Pneumol. Clin.* **2016**, *72*, 221–227. [CrossRef] [PubMed]
71. Duffy, D.L.; Mitchell, C.A.; Martin, N.G. Genetic and environmental risk factors for asthma: A cotwin-control study. *Am. J. Respir. Crit. Care Med.* **1998**, *157*, 840–845. [CrossRef] [PubMed]
72. Horvath, A.; Balashazy, I.; Farkas, A.; Sarkany, Z.; Hofmann, W.; Czitrovszky, A.; Dobos, E. Quantification of airway deposition of intact and fragmented pollens. *Int. J. Environ. Health Res.* **2011**, *21*, 427–440. [CrossRef] [PubMed]
73. Liu, L.; Li, G.; Sun, Y.; Li, J.; Tang, N.; Dong, L. Airway wall thickness of allergic asthma caused by weed pollen or house dust mite assessed by computed tomography. *Respir. Med.* **2015**, *109*, 339–346. [CrossRef] [PubMed]
74. Von Mutius, E. Gene-environment interactions in asthma. *J. Allergy Clin. Immunol.* **2009**, *123*, 3–11. [CrossRef] [PubMed]
75. Vinhas, R.; Cortes, L.; Cardoso, I.; Mendes, V.M.; Manadas, B.; Todo-Bom, A.; Pires, E.; Verissimo, P. Pollen proteases compromise the airway epithelial barrier through degradation of transmembrane adhesion proteins and lung bioactive peptides. *Allergy* **2011**, *66*, 1088–1098. [CrossRef] [PubMed]

76. Tran, M.M.; Lefebvre, D.L.; Dharma, C.; Dai, D.; Lou, W.Y.W.; Subbarao, P.; Becker, A.B.; Mandhane, P.J.; Turvey, S.E.; Sears, M.R.; et al. Predicting the atopic march: Results from the Canadian Healthy Infant Longitudinal Development Study. *J. Allergy Clin. Immunol.* **2017**, *141*, 601–607. [CrossRef] [PubMed]
77. Bergmann, R.L.; Wahn, U.; Bergmann, K.E. The allergy march: From food to pollen. *Environ. Toxicol. Pharmacol.* **1997**, *4*, 79–83. [CrossRef]
78. Warner, J.A.; Jones, C.A.; Jones, A.C.; Warner, J.O. Prenatal origins of allergic disease. *J. Allergy Clin. Immunol.* **2000**, *105*, S493–S498. [CrossRef]
79. Leung, R.C.; Carlin, J.B.; Burdon, J.G.; Czarny, D. Asthma, allergy and atopy in Asian immigrants in Melbourne. *Med. J. Aust.* **1994**, *161*, 418–425. [PubMed]
80. Ventura, M.T.; Munno, G.; Giannoccaro, F.; Accettura, F.; Chironna, M.; Lama, R.; Hoxha, M.; Panetta, V.; Ferrigno, L.; Rosmini, F.; et al. Allergy, asthma and markers of infections among Albanian migrants to Southern Italy. *Allergy* **2004**, *59*, 632–636. [CrossRef] [PubMed]
81. Beggs, P.J. Impacts of climate change on aeroallergens: Past and future. *Clin. Exp. Allergy* **2004**, *34*, 1507–1513. [CrossRef] [PubMed]
82. De Jong, N.W.; Vermeulen, A.M.; Gerth van Wijk, R.; de Groot, H. Occupational allergy caused by flowers. *Allergy* **1998**, *53*, 204–209. [CrossRef] [PubMed]
83. Anguita, J.L.; Palacios, L.; Ruiz-Valenzuela, L.; Bartolome, B.; Lopez-Urbano, M.J.; Saenz de San Pedro, B.; Cano, E.; Quiralte, J. An occupational respiratory allergy caused by *Sinapis alba* pollen in olive farmers. *Allergy* **2007**, *62*, 447–450. [CrossRef] [PubMed]
84. Garcia-Ortega, P.; Bartolome, B.; Enrique, E.; Gaig, P.; Richart, C. Allergy to Diplotaxis erucoides pollen: Occupational sensitization and cross-reactivity with other common pollens. *Allergy* **2001**, *56*, 679–683. [CrossRef] [PubMed]
85. Hermanides, H.K.; Lahey-de Boer, A.M.; Zuidmeer, L.; Guikers, C.; van Ree, R.; Knulst, A.C. Brassica oleracea pollen, a new source of occupational allergens. *Allergy* **2006**, *61*, 498–502. [CrossRef] [PubMed]
86. Swierczyniska-Machura, D.; Krakowiak, A.; Palczynski, C. Occupational allergy caused by ornamental plants. *Med. Pr.* **2006**, *57*, 359–364. [PubMed]
87. Miesen, W.M.A.J.; Van der Heide, S.; Kerstjens, H.A.M.; Dubois, A.E.J.; de Monchy, J.G.R. Occupational asthma due to IgE mediated allergy to the flower Molucella laevis (Bells of Ireland). *Occup. Environ. Med.* **2003**, *60*, 701–703. [CrossRef] [PubMed]
88. Eire, M.A.; Pineda, F.; Losada, S.V.; de la Cuesta, C.G.; Villalva, M.M. Occupational rhinitis and asthma due to cedroarana (Cedrelinga catenaeformis Ducke) wood dust allergy. *J. Investig. Allergol. Clin. Immunol.* **2006**, *16*, 385–387. [PubMed]
89. Blanco, C.; Ortega, N.; Castillo, R.; Alvarez, M.; Dumpierrez, A.G.; Carrillo, T. Carica papaya pollen allergy. *Ann. Allergy Asthma Immunol.* **1998**, *81*, 171–175. [CrossRef]
90. Barbato, A.; Pisetta, F.; Norbiato, M.; Ragusa, A.; Mesirca, P.; Pesenti, P.; Marcer, G. Influence of aeroallergens on bronchial reactivity in children sensitized to grass pollens. *Ann. Allergy* **1986**, *56*, 138–141. [PubMed]
91. Tovey, E.R.; Almqvist, C.; Li, Q.; Crisafulli, D.; Marks, G.B. Nonlinear relationship of mite allergen exposure to mite sensitization and asthma in a birth cohort. *J. Allergy Clin. Immunol.* **2008**, *122*, 114–118. [CrossRef] [PubMed]
92. Lebel, B.; Bousquet, J.; Morel, A.; Chanal, I.; Godard, P.; Michel, F.B. Correlation between symptoms and the threshold for release of mediators in nasal secretions during nasal challenge with grass-pollen grains. *J. Allergy Clin. Immunol.* **1988**, *82*, 869–877. [CrossRef]
93. Twaroch, T.E.; Curin, M.; Valenta, R.; Swoboda, I. Mold allergens in respiratory allergy: From structure to therapy. *Allergy Asthma Immunol. Res.* **2015**, *7*, 205–220. [CrossRef] [PubMed]
94. D'Amato, G.; Spieksma, F.T. Aerobiologic and clinical aspects of mould allergy in Europe. *Allergy* **1995**, *50*, 870–877. [CrossRef] [PubMed]
95. Bernardis, P.; Agnoletto, M.; Puccinelli, P.; Parmiani, S.; Pozzan, M. Injective versus sublingual immunotherapy in Alternaria tenuis allergic patients. *J. Investig. Allergol. Clin. Immunol.* **1996**, *6*, 55–62. [PubMed]
96. Baxter, D.M.; Perkins, J.L.; McGhee, C.R.; Seltzer, J.M. A regional comparison of mold spore concentrations outdoors and inside "clean" and "mold contaminated" Southern California buildings. *J. Occup. Environ. Hyg.* **2005**, *2*, 8–18. [CrossRef] [PubMed]

97. Nolte, H.; Hébert, J.; Berman, G.; Gawchik, S.; White, M.; Kaur, A.; Liu, N.; Lumry, W.; Maloney, J. Randomized controlled trial of ragweed allergy immunotherapy tablet efficacy and safety in North American adults. *Ann. Allergy Asthma Immunol.* **2013**, *110*, 450–456. [CrossRef] [PubMed]
98. Weichenthal, S.; Lavigne, E.; Villeneuve, P.J.; Reeves, F. Airborne Pollen Concentrations and Emergency Room Visits for Myocardial Infarction: A Multicity Case-Crossover Study in Ontario, Canada. *Am. J. Epidemiol.* **2016**, *183*, 613–621. [CrossRef] [PubMed]
99. Durham, S.R.; Emminger, W.; Kapp, A.; de Monchy, J.G.; Rak, S.; Scadding, G.K.; Wurtzen, P.A.; Andersen, J.S.; Tholstrup, B.; Riis, B.; et al. SQ-standardized sublingual grass immunotherapy: Confirmation of disease modification 2 years after 3 years of treatment in a randomized trial. *J. Allergy Clin. Immunol.* **2012**, *129*, 717–725. [CrossRef] [PubMed]
100. Connell, J.T. Quantitative intranasal pollen challenges. 3. The priming effect in allergic rhinitis. *J. Allergy* **1969**, *43*, 33–44. [CrossRef]
101. Jacobs, R.L.; Andrews, C.P.; Ramirez, D.A.; Rather, C.G.; Harper, N.; Jimenez, F.; Martinez, H.; Manoharan, M.; Carrillo, A.; Gerardi, M.; et al. Symptom dynamics during repeated serial allergen challenge chamber exposures to house dust mite. *J. Allergy Clin. Immunol.* **2015**, *135*, 1071–1075. [CrossRef] [PubMed]
102. O'Hehir, R.E.; Varese, N.P.; Deckert, K.; Zubrinich, C.M.; van Zelm, M.C.; Rolland, J.M.; Hew, M. Epidemic Thunderstorm Asthma Protection with Five-grass Pollen Tablet Sublingual Immunotherapy. *Am. J. Respir. Crit. Care Med.* **2018**, *198*, 126–128. [CrossRef] [PubMed]
103. Subbarao, P.; Becker, A.; Brook, J.R.; Daley, D.; Mandhane, P.J.; Miller, G.E.; Turvey, S.E.; Sears, M.R. Epidemiology of asthma: Risk factors for development. *Expert Rev. Clin. Immunol.* **2009**, *5*, 77–95. [CrossRef] [PubMed]
104. Clifford, R.L.; Jones, M.J.; MacIsaac, J.L.; McEwen, L.M.; Goodman, S.J.; Mostafavi, S.; Kobor, M.S.; Carlsten, C. Inhalation of diesel exhaust and allergen alters human bronchial epithelium DNA methylation. *J. Allergy Clin. Immunol.* **2017**, *139*, 112–121. [CrossRef] [PubMed]
105. Gershwin, L.J. Infectious and Environmental Triggers of Asthma. In *Current Clinical Practice: Bronchial Asthma: A Guide for Practical Understanding and Treatment*, 5th ed.; Humana Press Inc.: Totowa, NJ, USA, 2006.
106. Parameswaran, K.; Hildreth, A.J.; Taylor, I.K.; Keaney, N.P.; Bansal, S.K. Predictors of asthma severity in the elderly: Results of a community survey in Northeast England. *J. Asthma* **1999**, *36*, 613–618. [CrossRef] [PubMed]
107. Anyo, G.; Brunekreef, B.; de Meer, G.; Aarts, F.; Janssen, N.A.H.; van Vliet, P. Early, current and past pet ownership: Associations with sensitization, bronchial responsiveness and allergic symptoms in school children. *Clin. Exp. Allergy* **2002**, *32*, 361–366. [CrossRef] [PubMed]
108. Galli, L.; Facchetti, S.; Raffetti, E.; Donato, F.; D'Anna, M. Respiratory diseases and allergic sensitization in swine breeders: A population-based cross-sectional study. *Ann. Allergy Asthma Immunol.* **2015**, *115*, 402–407. [CrossRef] [PubMed]
109. Waser, M.; von Mutius, E.; Riedler, J.; Nowak, D.; Maisch, S.; Carr, D.; Eder, W.; Tebow, G.; Schierl, R.; Schreuer, M.; et al. Exposure to pets, and the association with hay fever, asthma, and atopic sensitization in rural children. *Allergy* **2005**, *60*, 177–184. [CrossRef] [PubMed]
110. Gassner-Bachmann, M.; Wuthrich, B. Farmers' children suffer less from hay fever and asthma. *Dtsch. Med. Wochenschr.* **2000**, *125*, 924–931. [CrossRef] [PubMed]
111. Bjerg, A.; Ekerljung, L.; Eriksson, J.; Naslund, J.; Sjolander, S.; Ronmark, E.; Dahl, Å.; Holmberg, K.; Wennergren, G.; Torén, K.; et al. Increase in pollen sensitization in Swedish adults and protective effect of keeping animals in childhood. *Clin. Exp. Allergy* **2016**, *46*, 1328–1336. [CrossRef] [PubMed]
112. Leynaert, B.; Neukirch, C.; Jarvis, D.; Chinn, S.; Burney, P.; Neukirch, F. Does living on a farm during childhood protect against asthma, allergic rhinitis, and atopy in adulthood? *Am. J. Respir. Crit. Care Med.* **2001**, *164*, 1829–1834. [CrossRef] [PubMed]
113. Braun-Fahrlander, C.; Gassner, M.; Grize, L.; Neu, U.; Sennhauser, F.H.; Varonier, H.S.; Vuille, J.C.; Wüthrich, B. Prevalence of hay fever and allergic sensitization in farmer's children and their peers living in the same rural community. SCARPOL team. Swiss Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution. *Clin. Exp. Allergy* **1999**, *29*, 28–34. [CrossRef] [PubMed]
114. Stein, M.M.; Hrusch, C.L.; Gozdz, J.; Igartua, C.; Pivniouk, V.; Murray, S.E.; Ledford, J.G.; Marques dos Santos, M.; Anderson, R.L.; Metwali, N.; et al. Innate Immunity and Asthma Risk in Amish and Hutterite Farm Children. *N. Engl. J. Med.* **2016**, *375*, 411–421. [CrossRef] [PubMed]

115. Klopp, A.; Vehling, L.; Becker, A.B.; Subbarao, P.; Mandhane, P.J.; Turvey, S.E.; Lefebvre, D.L.; Sears, M.R.; Azad, M.B.; CHILD Study Investigators. Modes of Infant Feeding and the Risk of Childhood Asthma: A Prospective Birth Cohort Study. *J. Pediatr.* **2017**, *190*, 192–199. [CrossRef] [PubMed]
116. Dogaru, C.M.; Nyffenegger, D.; Pescatore, A.M.; Spycher, B.D.; Kuehni, C.E. Breastfeeding and Childhood Asthma: Systematic Review and Meta-Analysis. *Am. J. Epidemiol.* **2014**, *179*, 1153–1167. [CrossRef] [PubMed]
117. Azad, M.B.; Becker, A.B.; Guttman, D.S.; Sears, M.R.; Scott, J.A.; Kozyrskyj, A.L. Gut microbiota diversity and atopic disease: Does breast-feeding play a role? *J. Allergy Clin. Immunol.* **2013**, *131*, 247–248. [CrossRef] [PubMed]
118. Rosas, I.; McCartney, H.A.; Payne, R.W.; Calderón, C.; Lacey, J.; Chapela, R.; Ruiz-Velazco, S. Analysis of the relationships between environmental factors (aeroallergens, air pollution, and weather) and asthma emergency admissions to a hospital in Mexico City. *Allergy* **2007**, *53*, 394–401. [CrossRef]
119. North, M.L.; Soliman, M.; Walker, T.; Steacy, L.M.; Ellis, A.K. Controlled Allergen Challenge Facilities and Their Unique Contributions to Allergic Rhinitis Research. *Curr. Allergy Asthma Rep.* **2015**, *15*, 11. [CrossRef] [PubMed]
120. Barnes, C.; Pacheco, F.; Landuyt, J.; Hu, F.; Portnoy, J. Hourly variation of airborne ragweed pollen in Kansas City. *Ann. Allergy Asthma Immunol.* **2001**, *86*, 166–171. [CrossRef]
121. Weber, R.W. Meteorologic variables in aerobiology. *Aerobiology* **2003**, *23*, 411–422. [CrossRef]
122. Barnes, C.; Pacheco, F.; Landuyt, J.; Hu, F.; Portnoy, J. The effect of temperature, relative humidity and rainfall on airborne ragweed pollen concentrations. *Aerobiologia* **2001**, *17*, 61–68. [CrossRef]
123. Andrew, E.; Nehme, Z.; Bernard, S.; Smith, K. 6 Characteristics of thunderstorm asthma EMS attendances in Victoria, Australia. *BMJ Open* **2017**, *7* (Suppl. 3), A2–A3.
124. Cockcroft, D.W.; Davis, B.E.; Blais, C.M. Thunderstorm asthma: An allergen-induced early asthmatic response. *Ann. Allergy Asthma Immunol.* **2018**, *120*, 120–123. [CrossRef] [PubMed]
125. Lee, J.; Kronborg, C.; O'Hehir, R.E.; Hew, M. Who's at risk of thunderstorm asthma? The ryegrass pollen trifecta and lessons learnt from the Melbourne thunderstorm epidemic. *Respir. Med.* **2017**, *132*, 146–148. [CrossRef] [PubMed]
126. D'Amato, G.; Annesi Maesano, I.; Molino, A.; Vitale, C.; D'Amato, M. Thunderstorm-related asthma attacks. *J. Allergy Clin. Immunol.* **2017**, *139*, 1786–1787. [CrossRef] [PubMed]
127. D'Amato, G.; Holgate, S.T.; Pawankar, R.; Ledford, D.K.; Cecchi, L.; Al-Ahmad, M.; Al-Enezi, F.; Al-Muhsen, S.; Ansotegui, I.; Baena-Cagnani, C.E.; et al. Meteorological conditions, climate change, new emerging factors, and asthma and related allergic disorders. A statement of the World Allergy Organization. *World Allergy Organ. J.* **2015**, *8*, 25. [CrossRef] [PubMed]
128. D'Amato, G.; Cecchi, L. Effects of climate change on environmental factors in respiratory allergic diseases. *Clin. Exp. Allergy* **2008**, *38*, 1264–1274. [CrossRef] [PubMed]
129. Valero, A.; Justicia, J.L.; Anton, E.; Dordal, T.; Fernandez-Parra, B.; Lluch, M.; Montoro, J.; Navarro, A.M. Epidemiology of allergic rhinitis caused by grass pollen or house-dust mites in Spain. *Am. J. Rhinol. Allergy* **2011**, *25*, e123–e128. [CrossRef] [PubMed]
130. Canonica, G.W.; Ciprandi, G.; Pesce, G.P.; Buscaglia, S.; Paolieri, F.; Bagnasco, M. ICAM-1 on epithelial cells in allergic subjects: A hallmark of allergic inflammation. *Int. Arch. Allergy Immunol.* **1995**, *107*, 99–102. [CrossRef] [PubMed]
131. Ogi, K.; Takabayashi, T.; Sakashita, M.; Susuki, D.; Yamada, T.; Manabe, Y.; Fujieda, S. Effect of Asian sand dust on Japanese cedar pollinosis. *Auris Nasus Larynx* **2014**, *41*, 518–522. [CrossRef] [PubMed]
132. Weeke, E.R. Epidemiology of allergic diseases in children. *Rhinol. Suppl.* **1992**, *13*, 5–12. [PubMed]
133. D'Amato, G.; Liccardi, G.; D'Amato, M.; Holgate, S. Environmental risk factors and allergic bronchial asthma. *Clin. Exp. Allergy* **2005**, *35*, 1113–1124. [CrossRef] [PubMed]
134. Carinanos, P.; Sanchez-Mesa, J.A.; Prieto-Baena, J.C.; Lopez, A.; Guerra, F.; Moreno, C.; Domínguez, E.; Galan, C. Pollen allergy related to the area of residence in the city of Cordoba, south-west Spain. *J. Environ. Monit.* **2002**, *4*, 734–738. [CrossRef] [PubMed]
135. Knudsen, T.B.; Thomsen, S.F.; Ulrik, C.S.; Fenger, M.; Nepper-Christensen, S.; Backer, V. Season of birth and risk of atopic disease among children and adolescents. *J. Asthma* **2007**, *44*, 257–260. [CrossRef] [PubMed]
136. Vovolis, V.; Grigoreas, C.; Galatas, I.; Vourdas, D. Is month of birth a risk factor for subsequent development of pollen allergy in adults? *Allergy Asthma Proc.* **1999**, *20*, 15–22. [CrossRef] [PubMed]

137. Lowe, A.J.; Olsson, D.; Bråbäck, L.; Forsberg, B. Pollen exposure in pregnancy and infancy and risk of asthma hospitalization—A register based cohort study. *Allergy Asthma Clin. Immunol.* **2012**, *8*, 17. [CrossRef] [PubMed]
138. D'Amato, G.; Bergmann, K.C.; Cecchi, L.; Annesi-Maesano, I.; Sanduzzi, A.; Liccardi, G.; Vitale, C.; Stanziola, A.; D'Amato, M. Climate change and air pollution: Effects on pollen allergy and other allergic respiratory diseases. *Allergo J. Int.* **2014**, *23*, 17–23. [CrossRef] [PubMed]
139. Guinea, J.; Peláez, T.; Alcalá, L.; Bouza, E. Outdoor environmental levels of Aspergillus spp. conidia over a wide geographical area. *Med. Mycol.* **2006**, *44*, 349–356. [CrossRef] [PubMed]
140. Bosch-Cano, F.; Bernard, N.; Sudre, B.; Gillet, F.; Thibaudon, M.; Richard, H.; Badot, P.M.; Ruffaldi, P. Human exposure to allergenic pollens: A comparison between urban and rural areas. *Environ. Res.* **2011**, *111*, 619–625. [CrossRef] [PubMed]
141. Reid, C.E.; Gamble, J.L. Aeroallergens, allergic disease, and climate change: Impacts and adaptation. *EcoHealth* **2009**, *6*, 458–470. [CrossRef] [PubMed]
142. Ziska, L.H.; Gebhard, D.E.; Frenz, D.A.; Faulkner, S.; Singer, B.D.; Straka, J.G. Cities as harbingers of climate change: Common ragweed, urbanization, and public health. *J. Allergy Clin. Immunol.* **2003**, *111*, 290–295. [CrossRef] [PubMed]
143. Majd, A.; Chehregani, A.; Moin, M.; Gholami, M.; Kohno, S.; Nabe, T.; Shariatzade, M.A. The Effects of Air Pollution on Structures, Proteins and Allergenicity of Pollen Grains. *Int. J. Aerobiol.* **2004**, *20*, 111–118. [CrossRef]
144. Pasqualini, S.; Tedeschini, E.; Frenguelli, G.; Wopfner, N.; Ferreira, F.; D'Amato, G.; Ederli, L. Ozone affects pollen viability and NAD(P)H oxidase release from Ambrosia artemisiifolia pollen. *Environ. Pollut.* **2011**, *159*, 2823–2830. [CrossRef] [PubMed]
145. Raynor, G.S.; Ogden, E.C.; Hayes, J.V. Dispersion and Deposition of Ragweed Pollen from Experimental Sources. *J. Appl. Meteorol.* **1970**, *9*, 885–895. [CrossRef]
146. Ying, Z.; Tie, X.; Li, G. Sensitivity of ozone concentrations to diurnal variations of surface emissions in Mexico City: A WRF/Chem modeling study. *Atmos. Environ.* **2009**, *43*, 851–859. [CrossRef]
147. Lazić, L.; Urošević, M.A.; Mijić, Z.; Vuković, G.; Ilić, L. Traffic contribution to air pollution in urban street canyons: Integrated application of the OSPM, moss biomonitoring and spectral analysis. *Atmos. Environ.* **2016**, *141*, 347–360. [CrossRef]
148. Masiol, M.; Hopke, P.K.; Felton, H.D.; Frank, B.P.; Rattigan, O.V.; Wurth, M.J.; LaDuke, G.H. Analysis of major air pollutants and submicron particles in New York City and Long Island. *Atmos. Environ.* **2017**, *148*, 203–214. [CrossRef]
149. Takaro, T.K.; Knowlton, K.; Balmes, J.R. Climate change and respiratory health: Current evidence and knowledge gaps. *Expert Rev. Respir. Med.* **2013**, *7*, 349–361. [CrossRef] [PubMed]
150. Romieu, I.; Moreno-Macias, H.; London, S.J. Gene by Environment Interaction and Ambient Air Pollution. *Proc. Am. Thorac. Soc.* **2010**, *7*, 116–122. [CrossRef] [PubMed]
151. Peltre, G. Inter-relationship between allergenic pollens and air pollution. *Allergie Immunol.* **1998**, *30*, 324–326.
152. Zhang, X.; Hirota, J.A.; Yang, C.; Carlsten, C. Effect of GST variants on lung function following diesel exhaust and allergen co-exposure in a controlled human crossover study. *Free Radic. Biol. Med.* **2016**, *96*, 385–391. [CrossRef] [PubMed]
153. Alexis, N.E.; Zhou, H.; Lay, J.C.; Harris, B.; Hernandez, M.L.; Lu, T.-S.; Bromberg, P.A.; Diaz-Sanchez, D.; Devlin, R.B.; Kleeberger, S.R.; et al. The glutathione-S-transferase Mu 1 null genotype modulates ozone-induced airway inflammation in human subjects. *J. Allergy Clin. Immunol.* **2009**, *124*, 1222–1228. [CrossRef] [PubMed]
154. Boldogh, I. ROS generated by pollen NADPH oxidase provide a signal that augments antigen-induced allergic airway inflammation. *J. Clin. Investig.* **2005**, *115*, 2169–2179. [CrossRef] [PubMed]
155. Traidl-Hoffmann, C.; Kasche, A.; Menzel, A.; Jakob, T.; Thiel, M.; Ring, J.; Behrendt, H. Impact of pollen on human health: More than allergen carriers? *Int. Arch. Allergy Immunol.* **2003**, *131*, 1–13. [CrossRef] [PubMed]
156. Abou Chakra, O.; Rogerieux, F.; Poncet, P.; Sutra, J.-P.; Peltre, G.; Senechal, H.; Lacroix, G. Ability of pollen cytoplasmic granules to induce biased allergic responses in a rat model. *Int. Arch. Allergy Immunol.* **2011**, *154*, 128–136. [CrossRef] [PubMed]

157. North, M.L.; Jones, M.J.; Macisaac, J.L.; Morin, A.M.; Steacy, L.M.; Gregor, A.; Kobor, M.S.; Ellis, A.K. Blood and nasal epigenetics correlate with allergic rhinitis symptom development in the environmental exposure unit. *Allergy* **2018**, *73*, 196–205. [CrossRef] [PubMed]
158. Holtzman, M.J.; Byers, D.E.; Alexander-Brett, J.; Wang, X. The role of airway epithelial cells and innate immune cells in chronic respiratory disease. *Nat. Rev. Immunol.* **2014**, *14*, 686–698. [CrossRef] [PubMed]
159. Broms, K.; Norback, D.; Eriksson, M.; Sundelin, C.; Svardsudd, K. Prevalence and co-occurrence of parentally reported possible asthma and allergic manifestations in pre-school children. *BMC Public Health* **2013**, *13*, 764. [CrossRef] [PubMed]
160. Bachert, C.; Vignola, A.M.; Gevaert, P.; Leynaert, B.; Van Cauwenberge, P.; Bousquet, J. Allergic rhinitis, rhinosinusitis, and asthma: One airway disease. *Immunol. Allergy Clin. N. Am.* **2004**, *24*, 19–43. [CrossRef]
161. Bousquet, J.; Van Cauwenberge, P.; Khaltaev, N.; Aria Workshop Group; World Health Organization. Allergic rhinitis and its impact on asthma. *J. Allergy Clin. Immunol.* **2001**, *108*, S147–S334. [CrossRef] [PubMed]
162. Kim, H.; Bouchard, J.; Renzix, P. The link between allergic rhinitis and asthma: A role for antileukotrienes? *Can. Respir. J.* **2008**, *15*, 91–98. [CrossRef] [PubMed]
163. Egan, M.; Bunyavanich, S. Allergic rhinitis: The "Ghost Diagnosis" in patients with asthma. *Asthma Res. Pract.* **2015**, *1*, 8. [CrossRef] [PubMed]
164. Ciprandi, G.; Buscaglia, S.; Scordamaglia, A.; Canonica, G.W. Allergen-specific conjunctival challenge in asthma. An additional diagnostic tool to define sensitization. *Int. Arch. Allergy Immunol.* **1997**, *112*, 247–250. [CrossRef] [PubMed]
165. Boulay, M.-E.; Boulet, L.-P. Influence of natural exposure to pollens and domestic animals on airway responsiveness and inflammation in sensitized non-asthmatic subjects. *Int. Arch. Allergy Immunol.* **2002**, *128*, 336–343. [CrossRef] [PubMed]
166. Cantani, A. Asthma. In *Pediatric Allergy, Asthma and Immunology*; Springer: Berlin/Heidelberg, Germany, 2008; pp. 725–873. Available online: http://link.springer.com.proxy.lib.sfu.ca/chapter/10.1007/978-3-540-33395-1_11 (accessed on 18 July 2016).
167. Hesselmar, B.; Bergin, A.-M.; Park, H.; Hahn-Zoric, M.; Eriksson, B.; Hanson, L.-A.; Padyukov, L. Interleukin-4 receptor polymorphisms in asthma and allergy: Relation to different disease phenotypes. *Acta Paediatr.* **2010**, *99*, 399–403. [CrossRef] [PubMed]
168. World Health Organization. Asthma. World Health Organization: Geneva, Switzerland, 2017. Available online: http://www.who.int/news-room/fact-sheets/detail/asthma (accessed on 31 May 2018).
169. Hertzen, L.; Haahtela, T. Signs of reversing trends in prevalence of asthma. *Allergy* **2005**, *60*, 283–292. [CrossRef] [PubMed]
170. Keith, P.K.; Desrosiers, M.; Laister, T.; Schellenberg, R.R.; Waserman, S. The burden of allergic rhinitis (AR) in Canada: Perspectives of physicians and patients. *Allergy Asthma Clin. Immunol.* **2012**, *8*, 7. [CrossRef] [PubMed]
171. Government of Canada, S.C. Asthma, by Age Group and Sex (Percent). 2016. Available online: https://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/health49b-eng.htm (accessed on 31 May 2018).
172. Gershon, A.S.; Guan, J.; Wang, C.; To, T. Trends in Asthma Prevalence and Incidence in Ontario, Canada, 1996–2005: A Population Study. *Am. J. Epidemiol.* **2010**, *172*, 728–736. [CrossRef] [PubMed]
173. Asher, M.I.; Montefort, S.; Björkstén, B.; Lai, C.K.; Strachan, D.P.; Weiland, S.K.; Williams, H.; ISAAC Phase Three Study Group. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* **2006**, *368*, 733–743. [CrossRef]
174. Ismaila, A.S.; Sayani, A.P.; Marin, M.; Su, Z. Clinical, economic, and humanistic burden of asthma in Canada: A systematic review. *BMC Pulm. Med.* **2013**, *13*, 70. [CrossRef] [PubMed]
175. Statistics Canada. Population by Sex and Age Group, Population as of July 1. Statistics Canada, CANSIM, Table 051-0001. 2016. Available online: http://www.statcan.gc.ca/tables-tableaux/sum-som/l01/cst01/demo10a-eng.htm (accessed on 18 October 2016).
176. Lavigne, E.; Gasparrini, A.; Stieb, D.M.; Chen, H.; Yasseen, A.S.; Crighton, E.; To, T.; Weichenthal, S.; Villeneuve, P.J.; Cakmak, S.; et al. Maternal Exposure to Aeroallergens and the Risk of Early Delivery. *Epidemiology* **2017**, *28*, 107–115. [CrossRef] [PubMed]
177. Dales, R.E.; Cakmak, S.; Judek, S.; Coates, F. Tree pollen and hospitalization for asthma in urban Canada. *Int. Arch. Allergy Immunol.* **2008**, *146*, 241–247. [CrossRef] [PubMed]

178. Dales, R.E.; Cakmak, S.; Burnett, R.T.; Judek, S.; Coates, F.; Brook, J.R. Influence of ambient fungal spores on emergency visits for asthma to a regional children's hospital. *Am. J. Respir. Crit. Care Med.* **2000**, *162*, 2087–2090. [CrossRef] [PubMed]
179. Héguy, L.; Garneau, M.; Goldberg, M.S.; Raphoz, M.; Guay, F.; Valois, M.-F. Associations between grass and weed pollen and emergency department visits for asthma among children in Montreal. *Environ. Res.* **2008**, *106*, 203–211. [CrossRef] [PubMed]
180. Cakmak, S.; Dales, R.E.; Burnett, R.T.; Judek, S.; Coates, F.; Brook, J.R. Effect of airborne allergens on emergency visits by children for conjunctivitis and rhinitis. *Lancet* **2002**, *359*, 947–948. [CrossRef]
181. Dales, R.E.; Cakmak, S.; Judek, S.; Dann, T.; Coates, F.; Brook, J.R.; Burnett, R.T. Influence of outdoor aeroallergens on hospitalization for asthma in Canada. *J. Allergy Clin. Immunol.* **2004**, *113*, 303–306. [CrossRef] [PubMed]
182. Tavakoli, H.; Fitzgerald, J.M.; Chen, W.; Lynd, L.; Kendzerska, T.; Aaron, S.; Gershon, A.; Marra, C.; Sadatsafavi, M.; Canadian Respiratory Research Network. Ten-year trends in direct costs of asthma: A population-based study. *Allergy* **2017**, *72*, 291–299. [CrossRef] [PubMed]
183. To, T.; Cicutto, L.; Degani, N.; McLimont, S.; Beyene, J. Can a community evidence-based asthma care program improve clinical outcomes? A longitudinal study. *Med. Care* **2008**, *46*, 1257–1266. [CrossRef] [PubMed]
184. Canadian Institute for Health Information. Asthma Emergency Department Visits: Volume and Median Length of Stay. 2015. Available online: http://indicatorlibrary.cihi.ca/display/HSPIL/Asthma+Emergency+Department+Visits%3A+Volume+and+Median+Length+of+Stay (accessed on 31 May 2018).
185. Theriault, L.; Hermus, G.; Goldfarb, D.; Stonebridge, C.; Bounajm, B. Cost Risk Analysis for Chronic Lung Disease in Canada. 2012. Available online: http://www.conferenceboard.ca/e-library/abstract.aspx?did=4585&AspxAutoDetectCookieSupport=1 (accessed on 31 May 2018).
186. Ariano, R.; Canonica, G.W.; Passalacqua, G. Possible role of climate changes in variations in pollen seasons and allergic sensitizations during 27 years. *Ann. Allergy Asthma Immunol.* **2010**, *104*, 215–222. [CrossRef] [PubMed]
187. Intergovernmental Panel on Climate Change. *Climate Change 2014 Impacts, Adaptation, and Vulnerability Part A: Global and Sectoral Aspects*; Cambridge University Press: New York, NY, USA, 2014.
188. Ziska, L.H.; Beggs, P.J. Anthropogenic climate change and allergen exposure: The role of plant biology. *J. Allergy Clin. Immunol.* **2012**, *129*, 27–32. [CrossRef] [PubMed]
189. Bonofiglio, T.; Orlandi, F.; Ruga, L.; Romano, B.; Fornaciari, M. Climate change impact on the olive pollen season in Mediterranean areas of Italy: Air quality in late spring from an allergenic point of view. *Environ. Monit. Assess.* **2013**, *185*, 877–890. [CrossRef] [PubMed]
190. Rice, M.B.; Thurston, G.D.; Balmes, J.R.; Pinkerton, K.E. Climate Change. A Global Threat to Cardiopulmonary Health. *Am. J. Respir. Crit. Care Med.* **2014**, *189*, 512–519. [CrossRef] [PubMed]
191. D'Amato, G.; Pawankar, R.; Vitale, C.; Lanza, M.; Molino, A.; Stanziola, A.; Vatrella, A.; D'Amato, M. Climate Change and Air Pollution: Effects on Respiratory Allergy. *Allergy Asthma Immunol. Res.* **2016**, *8*, 391–395. [CrossRef] [PubMed]
192. Emberlin, J.; Detandt, M.; Gehrig, R.; Jaeger, S.; Nolard, N.; Rantio-Lehtimaki, A. Responses in the start of Betula (birch) pollen seasons to recent changes in spring temperatures across Europe. *Int. J. Biometeorol.* **2002**, *46*, 159–170. [PubMed]
193. Stach, A.; Garcia-Mozo, H.; Prieto-Baena, J.C.; Czarnecka-Operacz, M.; Jenerowicz, D.; Silny, W.; Galán, C. Prevalence of Artemisia species pollinosis in western Poland: Impact of climate change on aerobiological trends, 1995–2004. *J. Investig. Allergol. Clin. Immunol.* **2007**, *17*, 39–47. [PubMed]
194. Takaro, T.; Henderson, S. Climate change and the new normal for cardiorespiratory disease. *Can. Respir. J.* **2015**, *22*, 1–4. [CrossRef] [PubMed]
195. Ahdoot, S.; Pacheco, S.E. Global Climate Change and Children's Health. Pediatrics. 26 October 2015. Available online: http://pediatrics.aappublications.org/content/early/2015/10/21/peds.2015-3233.abstract (accessed on 31 March 2017).
196. Ariano, R.; Berra, D.; Chiodini, E.; Ortolani, V.; Cremonte, L.G.; Mazzarello, M.G.; Galdi, E.; Calosso, C.; Ciprandi, G. Ragweed allergy: Pollen count and sensitization and allergy prevalence in two Italian allergy centers. *Allergy Rhinol.* **2015**, *6*, 177–183. [CrossRef] [PubMed]

197. Taylor, P.E.; Jacobson, K.W.; House, J.M.; Glovsky, M.M. Links between pollen, atopy and the asthma epidemic. *Int. Arch. Allergy Immunol.* **2007**, *144*, 162–170. [CrossRef] [PubMed]
198. Shea, K.M.; Truckner, R.T.; Weber, R.W.; Peden, D.B. Climate change and allergic disease. *J. Allergy Clin. Immunol.* **2008**, *122*, 443–453. [CrossRef] [PubMed]
199. Singer, B.D.; Ziska, L.H.; Frenz, D.A.; Gebhard, D.E.; Straka, J.G. Increasing Amb a 1 content in common ragweed (Ambrosia artemisiifolia) pollen as a function of rising atmospheric CO_2 concentration. *Funct. Plant Biol.* **2005**, *32*, 667–670. [CrossRef]
200. Sommer, J.; Plaschke, P.; Poulsen, L.K. Allergic disease—Pollen allergy and climate change. *Ugeskr. Laeger* **2009**, *171*, 3184–3187. [PubMed]
201. Lougheed, M.D.; Lemière, C.; Dell, S.D.; Ducharme, F.M.; FitzGerald, J.M.; Leigh, R.; Licskai, C.; Rowe, B.H.; Bowie, D.; Becker, A.; et al. Canadian Thoracic Society Asthma Management Continuum—2010 Consensus Summary for Children Six Years of Age and Over, and Adults. *Can. Respir. J.* **2010**, *17*, 15–24. [CrossRef] [PubMed]
202. Johnston, F.H.; Wheeler, A.J.; Williamson, G.J.; Campbell, S.L.; Jones, P.J.; Koolhof, I.S.; Lucani, C.; Cooling, N.B.; Bowman, D.M.J.S. Using smartphone technology to reduce health impacts from atmospheric environmental hazards. *Environ. Res. Lett.* **2018**, *13*, 044019. [CrossRef]
203. Magnan, A.; Romanet, S.; Vervloet, D. Asthma and allergy. *Rev. Prat.* **2001**, *51*, 511–516. [PubMed]
204. D'Amato, G.; Liccardi, G.; D'Amato, M.; Cazzola, M. The role of outdoor air pollution and climatic changes on the rising trends in respiratory allergy. *Respir. Med.* **2001**, *95*, 606–611. [CrossRef] [PubMed]
205. Palma-Gomez, S.; Gonzalez-Diaz, S.N.; Arias-Cruz, A.; Macias-Weinmann, A.; Amaro-Vivian, L.E.; Perez-Vanzzini, R.; Gutiérrez-Mujica, J.J.; Yong-Rodríguez, A. Effects of reforestation on tree pollen sensitization in inhabitants of Nuevo Leon, Mexico. *Rev. Alerg. Méx.* **2014**, *61*, 162–167. [PubMed]

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Table S1. Plant-Derived Aeroallergens in the Major Floristic Zones of Canada

Floristic Zone	Trees		Grasses and Weeds	
	Common Name	**Genus**	**Common Name**	**Genus**
Northwest Coastal: Southwestern British Columbia (BC)	Cedar	*Juniperus*	Rye & Orchard grass	*Lolium & Dactylis*
	Fir	*Abies*	Fescue grass	*Festuca*
	Pine	*Pinus*	Brome/chess grass	*Bromus*
	Alder	*Alnus*	Timothy & velvet grass	*Phleum & Holcus*
	Birch	*Betula*	Sweet grass	*Anthoxanthum*
	Hazel	*Corylus*	Plantain & Amaranths	*Plantago & Amaranthus*
	Oak	*Quercus*	Short ragweed	*Ambrosia*
	Cypress	*Cupressaceae*	Chenopods & Orach	*Kochia & Atriplex*
			Dock & Sorrel	*Rumex*
Northern Forest : Yukon, NWT, Nunavut, Newfoundland and Labrador, Northern BC, Alberta, Manitoba, Ontario & Quebec	Juniper	*Juniperus*	Mugwort	*Artemisia*
	Cedar & Birch	*Cedrus& Betula*	Nettle	*Urtica*
	Pine & Fir	*Pinus & Abies*	Chenopods	*Chenopdium & Kochia*
	Alder & Aspen	*Alnus & Populus*	Pigweeds	*Amaranthus*
	Willow & Maple	*Salix & Acer*	Pasture grasses (*low)*	
Rocky Mountain: Southeastern BC, Southern Alberta	Mountain cedar	*Juniperus*	Rye & Orchard grass	*Lolium & Dactylis*
	Pine	*Pinus*	Fescue grass	*Festuca*
	Aspen/Cottonwood	*Populus*	Timothy & Chess grass	*Bromus & Phleum*
	Willow	*Salix*	Tumbleweeds	*Kochia & Salsol*
	Maple/Boxelder	*Acer*	Pigweed	*Amaranthus*
	Oak	*Quercus*	Dock & Sage	*Rumex & Artemisia*
	Ash	*Fraxinus*	Giant/western ragweed	*Ambrosia*
Central Plains: Southern Alberta, Saskatchewan and Manitoba	Red cedar	*Juniperus*	Rye & Orchard grass	*Lolium & Dactylis*
	Pine & Beech	*Pinus & Fagus*	Fescue grass	*Festuca*
	Red/white oak	*Quercus*	Timothy & chess grass	*Phleum & Bromus*
	Elm & Ash	*Ulmus & Fraxinus*	Sweet grass	*Anthoxanthum*
	Maple/Box elder	*Acer*	Short/giant ragweed	*Ambrosia*
	Alder & Birch	*Alnus & Betula*	Mugwort	*Artemisia*
	Walnut & Pecan	*Juglans*	Pigweed	*Amaranthus*
	Locust &Hawthorn	*Robinia &Crategus*	Lamb's quarter	*Chenopodium*
	Cottonwood	*Populus*	Nettle & Dock/sorrel	*Urtica & Rumex*
	Willow & Locust	*Salix & Robina*	Plantain & Chenopods	*Plantago & Kochia*
	Sycamore&Hickory	*Plantanus & Carya*	Pigweed & Waterhemp	*Amaranthus & Ancida*
Eastern Agricultural: Southern Ontario, Southern Quebec, New Brunswick, Nova Scotia, Prince Edward Island	Cedar & Pine	*Juniperus & Pinus*	Rye & Orchard grass	*Lolium & Dactylis*
	Oak & Beech	*Quercus & Fagus*	Fescue & chess grass	*Festuca & Bromus*
	Elm & Ash	*Ulmus & Fraxinus*	Timothy & Sweet grass	*Phleum&Anthoxanthum*
	Sycamore	*Plantanus*	Short/giant ragweed	*Ambrosia*
	Maple & Cypress	*Acer&Cupressaceae*	Mugwort & Pigweed	*Artemisia&Amaranthus*
	Alder & Birch	*Alnus & Betula*	Lamb's quarter	*Chenopodium*
	Hickory & Locust	*Carya & Robinia*	Dock & sorrel	*Rumex*
	Hawthorn	*Crategus*	Plantain & Nettle	*Plantago & Urtica*
	Walnut & Pecan	*Juglans*		

Adapted from [14].