Ragweed as an Example of Worldwide Allergen Expansion

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Multiple factors are contributing to the expansion of ragweed on a worldwide scale. This review seeks to examine factors that may contribute to allergen expansion with reference to ragweed as a well-studied example. It is our hope that increased surveillance for new pollens in areas not previously affected and awareness of the influence the changing environment plays in allergic disease will lead to better outcomes in susceptible patients.

Key words: *allergens, allergen expansion, CO_2, global warming, ozone, ragweed*

Multiple factors are contributing to the expansion of allergens on a worldwide scale. Increased travel and trade have led to the introduction of certain allergenic species to other environments that had never seen them previously.[1] These include pollens from many plant species that are new to these environments. The climate changes that are occurring owing to global warming may serve as another influence that will allow new allergens to expand into different regions in the future. These changes include the increasing length of the growing seasons, changes in agricultural practices, ozone exposure, and increased atmospheric CO_2 levels. Exposure to air pollutants has been repeatedly shown to influence the immune system's response to allergens.[2,3] Long-distance transport of *anemophilus* pollens could represent a source of pollen exposure for inhabitants in areas in which the species are not present in sufficient quantities to invoke symptoms.[1,4,5] As allergy sufferers are exposed to increasing amounts of air pollution in the future, this could lead to increased sensitization and thus symptoms. Increased allergen exposure may have a number of detrimental effects on the exposed population related to higher rates of sensitization. Sensitization in children can lead to the classic "allergic march," which includes a progression from atopic dermatitis and/or allergic rhinitis to asthma.[6] In adults, new allergen sensitization may increase the development of allergic disease, with persistence of symptoms into older adulthood or asymptomatic sensitization that does not develop clinically until later in life.[7] This notion is supported by the change in prevalence for allergic rhinitis in the US population from 10% in 1970 to 30% in 2000.[8] In addition to asthma and rhinitis, allergic sensitization also increases the rates of rhinosinusitis.[9] The prevalence of drug allergy, food allergy, and anaphylaxis may also be increased since atopic sensitization is a risk factor for all of these maladies.[8] Only with specific knowledge of the etiology and implications of these changes can researchers and physicians maximally assist allergic patients. The purpose of this review is to examine factors that may contribute to allergen expansion, with specific reference to ragweed as a well-studied example.

Ragweed as an Example of Allergen Expansion

Ragweed serves as a novel allergenic species that has expanded on a global scale. Recent studies of this pollen and its allergenic potentials serve to illustrate the possible future impact of major climate changes.

Plants of the genus *Ambrosia* (ragweed) belong to the Asteraceae family. There are 22 known allergens, with 6 considered major.[10] In North America, 17 species of ragweed have been discovered.[11] The only native species in Europe is *Ambrosia maritima* L., but four other species, *Ambrosia artemisiifolia* L. (short or common ragweed), *Ambrosia coronopifolia*, *Ambrosia tenuifolia*, and *Ambrosia trifida* L., have all been introduced from other locations.[12] *Ambrosia artemisiifolia* is one of the most common causes of respiratory allergy in North America. The pollen is

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tricolporate, with a spiny, granular surface.[13] It tends to grow in large numbers, and a single plant can release about 1 billion pollen grains in a season.[14] The plants grow to about 1.2 metres in height and have pollen grains that are about 15 to 25 μm in size.[15] Although most larger pollen grains cannot deposit deep in the peripheral airways, it has been demonstrated that ragweed pollen exists in particle sizes of less than 10 μm[16–18] that could potentially lead to lower respiratory symptoms. It was recently reported that subpollen particles released from ragweed pollen grains, ranging in size from 0.5 to 4.5 μm, could induce allergic inflammation in an animal model.[19]

It has been estimated that symptoms after exposure to ragweed pollen can begin with concentrations of as few as 5 to 20 pollen grains/m^3.[20,21] In the midwestern United States, the typical pollen count during ragweed season is about 200 grains/m^3.[22]

Ragweed tends to grow in fields and in freshly cleared grounds. It is considered an annual disturbance weed that completes its life cycle in 1 year and requires the clearing or disturbance of the soil for future growth.[14] The expansion of ragweed in both the United States and Europe has been attributed to increasing deforestation and economic development.[12]

Ragweed in North America

It is believed that ragweed originated in South America and flourished in the United States when more grounds were disturbed during expansion. Ragweed also was a significant problem in the slums and vacant lots in heavily industrialized cities.[23] Early twentieth century efforts to "eradicate" ragweed from several regions in the United States were unsuccessful, and now ragweed represents one of the major national allergens.

In the recent National Health and Nutrition Examination Survey (NHANES) III (1988–1994), 26.2% of the US population was sensitized to ragweed, the third most common allergen after dust mites (27.5%) and perennial rye grass (26.9%).[24] This prevalence was increased from 10% of the population in NHANES II (1976–1980).[25] Ragweed is also a major allergen in Canada. In a series of 3,371 atopic patients, Boulet and colleagues discovered that 44.9% were sensitized to ragweed.[26]

Expansion of Ragweed Worldwide

The expansion of ragweed species into European countries has been well chronicled. The Carpathian Basin in Hungary is an area that reports some of the highest ragweed pollen concentrations in Europe, with counts that were 77 to 87% of the total pollen count during the 1 month of highest release from 1997 to 2001.[27]

Ragweed is thought to have been introduced into France with potato sacks, American war supplies, and cereal sacks in the 1930s to 1960s.[10] The Rhone-Alps and Burgandy regions are considered to be the areas in France that have been affected the most.[28] Laaidi and colleagues investigated pollen counts in the city of Lyon between 1987 and 2001.[10] Data revealed a rising trend, with 143 to 403 grains/m^3 maximum between 1994 and 2001, increased from 19 to 126 grains/m^3 during 1987 to 1993.

Ragweed is also an increasing problem in Italy.[29] Asero reported a trend toward ragweed sensitization at a younger age in areas of northern Italy over the last few years.[30] This is in contrast to his earlier finding that most ragweed-sensitized individuals in the area were over 35 years old,[31] stressing the point that the evolving expansion of ragweed is greatly affecting patients in the area.

Ragweed pollen counts at three sites in central Croatia during 2002 to 2003 were greater than 30 grains/m^3 for 19 to 45 days in 2002 and 30 to 54 days in 2003. This represented the third most abundant pollen type in that study.[32] In northeastern Croatia, ragweed pollen was present in concentrations greater than 10 grains/m^3 for 51, 44, and 35 days during the 2001–2003 seasons. The maximum daily concentration in this study was 528 grains/m^3.[33] In southern Croatia, 47% of 120 patients who had symptoms and positive skin tests during the ragweed season reacted to *Ambrosia* in 2003. Ragweed pollen represented a maximum of 12% of the total weekly pollen count during the peak season.[34]

Analysis of pollen counts in the Czech Republic between 1992 and 1997 revealed significant levels of pollen only occasionally from the station in Brno.[35] Incidentally, in the same study, a skin-prick test or specific IgE by radioallergosorbent test in a group of over 200 adults each year between 1995 and 1997 in Brno revealed 19 to 25% to be sensitized to ragweed.

In Switzerland, there has been an increasing trend in measured ragweed pollen counts in Geneva since sampling was started in 1979. Although the number of ragweed-sensitized patients in the Geneva area is low, there are cases that have been related to local sensitization.[12] It is thought that imported contaminated birdseed is a major source of ragweed introduction into Sweden.[1] Ragweed has also been noted in Austria,[36] Bulgaria,[37] Poland,[38] and Slovakia.[39]

Environmental Factors

Long-Distance Transport

Owing to the small size of the ragweed pollen grain, the ability of the pollen to travel long distances has been studied by a number of researchers. Although ragweed species are not present in the areas of central Italy, Cecchi and colleagues reported increased collection over the period from 1999 to 2004 in the areas of Florence and Pistoia.[4] Between August 20 and September 20 over the last 3 years of the study, the levels were above 10 grains/m^3 for 80 to 90% of the time.[4] A study by Stach and colleagues calculated the amount of *Ambrosia* pollen in the Poznan area of Poland between 1995 and 2005.[5] It was shown by back-trajectory analysis that it was possible that long-range transport from southern Poland, Slovakia, Hungary, and the Czech Republic could be attributed to the observed ragweed pollen counts. There were 18 days during the study in which the counts were greater than 20 grains/m^3. Other studies have also noted that long-range transport of ragweed pollen can occur.[1,40]

Effects of Agriculture

Local agricultural practices can influence the types of plants that are able to survive and proliferate in an area. The expansion of ragweed has been attributed to changes in agricultural practice. In their study of ragweed in France, Laaidi and colleagues postulated that the European Common Agricultural Policy that required farmers to leave part of their land lying fallow increased this potential source of ragweed growth.[10] They also suggested that an increase in sunflower crops in the area could have increased proliferation of ragweed because they both belong to the Asteraceae family and grow well together and because herbicides cannot be used on ragweed owing to fear of destroying the sunflower crops.

Effects of Higher CO_2 Levels

It has been predicted that atmospheric CO_2 levels will increase in the future as a result of global climate change.[41,42] A few studies have attempted to explore the impact of this predicted change on the growth and pollen production of ragweed. Ziska and Caulfield found that higher CO_2 concentrations yielded elevated levels of pollen production and biomass from ragweed.[43] Wayne and colleagues also noted that ragweed pollen production was 61% higher in plants grown in elevated CO_2 environments, a finding that might suggest that ragweed pollen production could increase as global warming progresses.[44] In an experiment using the differences between urban and rural environments as a surrogate for possible future climate changes, Ziska and colleagues found that greater ragweed biomass and atmospheric pollen counts were encountered in the urban area. The urban area had 30 to 31% higher average daily CO_2 concentrations and a 1.9°C temperature increase relative to the rural site.[45] They also noted that ragweed flowered earlier in urban compared with rural sites.

Length of Seasons

It has been postulated that the changing environment, particularly the trend of global warming, may lead to increased pollen exposure and expanded environments for growth of numerous plant species.[21] An increase in the growing season with earlier flowering and possible increased airborne pollen counts could be consequences of the projected rise in temperature. A number of studies addressing plant and animal phenophases (recurrence of annual phenomena such as plant budding) have been performed. Polar areas or areas of colder climates seem to be particularly susceptible to warming, as evidenced by studies of plant phenophases in these areas.[46] In a phenologic survey in southern Wisconsin with events recorded over a 61-year period, it was determined that the mean of regressions for the 55 phenophases studied was -0.12 days per year.[47] In a review of phonologic events in Europe with data from the International Phenological Gardens over a 30-year period, Menzel noted a lengthening of the growing season by +0.36 day/year (an advancement of spring by 6.3 days and a delay in fall of 4.3 days).[48] It was also noted in this study that the advancement was more pronounced in areas of northern and central Europe. With respect to the ragweed plant, this trend might be relevant to areas in which the current vegetation period is too short to allow full seed maturity, such as Sweden.[1]

In a comparison of ragweed plants released from dormancy at three 15-day intervals, Rogers and colleagues determined that the plants released from dormancy first had increased height, increased weight, and 54.8% greater production of pollen compared with plants released at the last interval.[49] These data suggest that ragweed pollen production might increase with the earlier onset of spring and longer growing season that will accompany climactic changes in the future.

Other pollens have also been studied in relation to the lengthening of the growing season. Emberlin and colleagues looked at birch pollen start dates and temperatures from six European cities over the 1982–1999 time period and used regression analysis to predict future trends.[50] It was noted that most of the sites showed earlier start dates, with a postulated 6-day increase in pollen start dates over the next 10 years if trends continue. Data from Switzerland indicate that birch pollen appears 3 weeks and ash pollen 1 week earlier than 20 years previously.[51] Researchers using a climate change model based on predicted meteorologic changes and past *Quercus* pollen data in the Iberian Peninsula area of Spain postulated that the pollination season could begin as much as 1 month earlier, with as much as a 50% greater airborne pollen concentration by the end of the twenty-first century.[52]

Environmental Interactions

Although the expansion of allergens worldwide has led to increased numbers of individuals who have been sensitized, the exposure of these individuals to environmental changes and air pollution might also lead to increased disease activity. One such example is the exposure of allergic patients to increasing amounts of ozone. In a study of mild asthmatics with sensitivity to *Dermatophagoides farinae* by Peden and colleagues, exposure to ozone levels of 0.16 ppm for 7.6 hours yielded a significant increase in both eosinophils and neutrophils in bronchoalveolar lavage fluid sampled at 18 hours after exposure.[53] Ozone exposure also resulted in a significant decrease in both forced vital capacity and forced expiratory volume in 1 second in this group of patients. The effect of exposure to diesel exhaust particles (DEPs) in allergic patients has also been studied by a number of researchers. Dust mite–sensitive patients who were challenged with 0.3 mg of DEPs prior to allergen exposure yielded a dramatic increase in nasal symptom scores that correlated with histamine levels in nasal lavage fluid.[2] In another study in ragweed-sensitive rhinitis patients, the combination of ragweed and DEP exposure yielded a statistically significant increase in the amount of ragweed-specific IgE in nasal lavage compared with ragweed exposure alone.[3]

Conclusion

Ragweed serves as an ideal example for discussing the spread of allergens on an international scale and illustrating the effects of the changing environment on allergic disease. With the prevalence of allergic diseases increasing,[54] it becomes important to study these confounding factors that increase sensitization and/or symptoms so that effective interventions can be designed and implemented. The observations that the growing seasons appear to be increasing in length could have dramatic implications for expansion of allergenic plants into regions with colder climates and the level of pollens in areas where the species already exists in adequate numbers. Studies with ragweed have also shown that airborne spread to regions in which the species is not prevalent could lead to a significant number of days with sufficient levels of exposure to produce allergic symptoms.[4,5] Exposure to ozone and air pollution has also been shown to influence allergic disease. Given that DEPs are significant components of the air in most industrialized countries,[3] the recent studies linking DEPs to increased indices of allergic disease are very concerning. It is hoped that increased surveillance for new pollens in areas not previously affected and awareness of the environmental influence on patients with allergic disease will lead to better prevention of allergic sensitization and control of symptoms in susceptible patients.

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