



Review of the Impacts
of Climate Variability
and Change on Aeroallergens
and Their Associated Effects

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A Review of the Impacts of Climate Variability and
Change on Aeroallergens and
Their Associated Effects

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LIST OF ABBREVIATIONS

A&E	Accident and Emergency
AAAAI	American Academy of Allergy Asthma and Immunology
BLS CPI	Bureau of Labor Statistics Consumer Price Index
CCF	Climate Change Futures
CDC	Centers for Disease Control and Prevention
COI	cost of illness
DALY	disability adjusted life years
ED	emergency department
ENSO	El Niño-Southern Oscillation
GCMs	general circulation models
GCRP	Global Change Research Program
IPCC	Intergovernmental Panel on Climate Change
JCAAI	Joint Council of Allergy, Asthma and Immunology
NAST	National Assessment Synthesis Team
NCHS	National Center for Health Statistics
ORD	Office of Research and Development
PEFRs	peak expiratory flow rates
U.S. EPA	U.S. Environmental Protection Agency
WTP	willingness to pay

PREFACE

The Environmental Protection Agency's Global Change Research Program (GCRP) is an assessment-oriented program within the Office of Research and Development (ORD) that focuses on assessing how potential changes in climate and other global environmental stressors may impact air quality, water quality, ecosystems, and human health in the United States. The Program's focus on human health is consistent with the *Strategic Plan* of the U.S. Climate Change Science Program—the federal umbrella organization for climate change science in the U.S. government. It is responsive to the research agenda set out in the Health Sector Assessment of the First National Assessment of the Potential Consequences of Climate Variability and Change in the United States.

Since 1998, the National Center for Environmental Assessment within the ORD has assessed the consequences of global change on weather-related morbidity, on vector- and water-borne diseases, and on airborne allergens and ambient pollutants, especially tropospheric ozone and fine particles. Through its assessments, this Program has provided timely scientific information to stakeholders and policy makers to support them as they decide whether and how to respond to the risks and opportunities presented by climate change.

Because health is affected by a variety of social, economic, political, environmental, and technological factors, assessing the health impacts of global change is a complex challenge. As a result, health assessments in the GCRP look beyond epidemiological and toxicological research to develop integrated health assessment frameworks that consider the effects of multiple stresses, their interactions, potential adaptive responses, and location-specific impacts. This report assesses the state of the scientific literature and examines the potential effects of climate variability and change on aeroallergens and their associated health outcomes in the United States.

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EXECUTIVE SUMMARY

This report presents a survey of the current state of knowledge of the potential impacts of climate change and variability on aeroallergens—pollen, mold, and indoor allergens—in the United States and the allergic diseases associated with them. Allergies are prevalent in the United States and impose substantial economic and quality-of-life burdens. A recent nationwide survey reported that 54.6% of people in the United States test positive for one or more allergens (American Academy of Allergy Asthma and Immunology [AAAAI], 1996–2005). Among specific allergens, dust mites, rye, ragweed, and cockroaches caused sensitization in approximately 25% of the population (Arbes et al., 2005).

Allergies are the sixth most costly chronic disease category in the United States, collectively costing the health care system approximately \$21 billion annually (AAAAI, 1996–2005). The three main allergic diseases that have been associated with exposure to aeroallergens—allergic rhinitis (hay fever), asthma, and atopic dermatitis (eczema)—individually and collectively impose both substantial health effects and large economic burdens. The direct medical costs of asthma and allergic rhinitis (hay fever) are estimated to be \$12.5 billion and \$6.2 billion per year, respectively (in 2005 U.S. dollars) (AAAAI, 1996–2005); the direct medical costs of atopic dermatitis (eczema) are estimated to be \$1.2–\$5.9 billion per year (in 2005 dollars) (Ellis et al., 2002).

While data suggest that aeroallergen levels have remained relatively stable, the prevalence of allergic diseases in the United States has increased over the last 30 years, a trend that appears to be mirrored in other countries as well. The causes of this upward trend are as yet unclear. Because the economic impacts of allergic diseases associated with aeroallergens and the quality-of-life impacts on those individuals who suffer from them are already substantial, any climate change-induced enhancement or continuation of this trend in the United States would be of particular concern.

General projections of climate change and potential impacts on aeroallergens

While climate change projections are uncertain, multiple efforts have been made to derive future climate scenarios based on projected concentrations of greenhouse gases and models that simulate the climate system. The United Nations Intergovernmental Panel on

Climate Change (IPCC) projects that by the year 2100, the annual surface temperature increases are projected to range from 1–3°C near the coasts in the conterminous United States to more than 5°C in northern Alaska (IPCC, 2007). Along with increasing temperatures, other effects of climate change, such as changes in precipitation and increases in extreme weather events, have also been anticipated. These changes, including increased CO₂ concentrations, could impact the production, distribution, and dispersion of aeroallergens along with the allergen content and the growth and distribution of the weeds, grasses, trees, and mold that produce them. Shifts in aeroallergen production and, subsequently, human exposure, may result in changes in the severity and prevalence of symptoms in individuals with allergenic illnesses suffering from allergic diseases.

The literature does not provide definitive data or conclusions, however, on how climate change might impact aeroallergens and, subsequently, the severity or prevalence of allergic diseases in the United States. This is, in part, because studies are of necessity often narrowly defined, and a single study is unlikely to encompass the broad subject of weather, aeroallergens, and allergic illness. There is also an inherent uncertainty as to how the climate will change, especially at a regional level. In addition, the etiology of allergic diseases, especially asthma, is complex and has a gene-environment interaction that is not yet well understood. Finally, there are numerous other factors that affect aeroallergen levels and the severity and prevalence of associated allergic diseases, such as changes in land use, air pollution, adaptive responses, and modifying factors; many of which are difficult to assess or characterize.

Nevertheless, some tentative conclusions can be drawn about the potential impact of climate change on aeroallergens and the associated allergic diseases through inferences regarding the links between (1) climate change and the characteristics of aeroallergens and (2) those aeroallergen characteristics and the associated allergic diseases.

Other research has shown that pre-season temperature and precipitation have been consistently important factors for pollen and mold production. Overall, experimental and observational data as well as models indicate the following likely changes in aeroallergen production, distribution, dispersal, and allergen content as a result of climate change in the United States:

- Pollen production is likely to increase in many parts of the United States, with the possible exception of the Southeast;
- Phenologic advance is likely to occur for numerous species of plants, especially trees (Root et al., 2003);
- There will likely be changes in the distribution of pollen-producing species, including the possibility of extinction in some cases (Joyce et al., 2001);
- Intercontinental dispersal (e.g., of pollen) is possible, facilitating the introduction of new aeroallergens into the United States (Husar et al., 2001); and
- Increases in allergen content, and thus, potency, of some aeroallergens are possible (Beggs, 2004; Beggs and Bambrick, 2005).

Research on the potential effects of climate change on tree and grass pollen production in the United States is limited, but there are more of these types of studies. In general, the literature to date suggests that pre-season temperature and precipitation are important projectors of both tree and grass pollen production. To the extent that climate change results in changes in these two meteorological variables, then we would expect corresponding changes in tree and grass pollen production, all else being equal. The evidence to date suggests that the nature of the changes may be region- and species-specific. Although this does not necessarily imply increased pollen production, a consistent finding from international research is earlier start dates for pollen seasons, especially in trees (Clot, 2003).

Among weed pollen, common ragweed (*Ambrosia artemisiifolia* L.) is recognized as a significant cause of allergic rhinitis (hay fever) in the United States and there is relatively more research on the response of this weed to climatic variables, especially in the context of climate change. Several researchers have used controlled environments to examine ragweed response to carbon dioxide levels and temperature, the two covariates for which models reliably project increased levels in the future. The experimental results have consistently demonstrated that doubling carbon dioxide levels from current (350 $\mu\text{mol/mol}$) to projected future levels (700 $\mu\text{mol/mol}$) would result in a 60 to 90% increase in ragweed pollen production (Ziska and Caulfield, 2000; Wayne et al., 2002). A field study demonstrated ragweed grew faster, flowered earlier, and produced significantly greater aboveground biomass and ragweed pollen at urban locations than at rural locations (Ziska et al., 2003). Because urban locations are warmer and have higher concentrations of CO_2 than rural locations, this may have implications for the impact

of climate change on ragweed pollen production overall. In summary, studies of ragweed in controlled environments and in field studies clearly show that pollen production can be expected to increase with increased temperature and carbon dioxide levels.

There is limited but inconsistent evidence of increasing trends in mold production. Assessment of mold production in response to climate change is derived mainly from observational analyses of long-term data sets. An analysis in Denver, Colorado showed *Cladosporium* increasing, but not co-occurring mold such as *Alternaria* or *Epicoccum* (Katial et al., 1997). An observational study in Derby, UK showed *Alternaria* increasing (Corden and Millington, 2001). Another United States study observed increases in mold counts after an El Niño event (Freye and Litwin, 2001). While the extent of the impact is not altogether understood, it is clear that climatic factors have an impact on mold production.

Long-term responses to climate change (over 50 to 100 years) are likely to include species' range or distribution shifts, and in some cases, possible extinction. Some ecological models suggest that the potential habitats, and thus distribution, for many tree species in the United States are likely to change, in some cases dramatically, by the end of the 21st century. Trees favoring cool environments, such as maple and birch, are likely to shift northward, possibly out of the United States entirely, thus altering the pollen distribution associated with them (Joyce et al., 2001). The habitats of alpine, subalpine spruce/fir, and aspen communities are likely to contract significantly in the United States and largely shift into Canada (Joyce et al., 2001). Potential habitats for oak/hickory, oak/pine, ponderosa pine, and arid woodland communities are likely to increase in the United States (Joyce et al., 2001). Under certain model scenarios, the Southeast will experience significant warming trends leading to an expansion of savannas and grasslands at the expense of forest, again altering the presence of major aeroallergens in large regions of the country. Note however, conclusions about projected shifts in the distribution of major vegetation types, as plant species move in response to climate change, depend on an implicit assumption in the biogeography models that contend that vegetation will be able to move freely from location to location. This assumption "may be at least in part unwarranted because of the barriers to plant migration that have been put in place on landscapes through agricultural expansion and urbanization" (Melillo et al., 2001, p. 82).

There has been only limited research on how climate change could affect the dispersal of pollen and mold, but there are cases of both pollen and dust being dispersed long distances from

their release sites. The frequency of such cases may be increased by climate change. One study, for example, suggests that in Europe, increased strength of westerly winds due to climate change will enhance the long-range transport of birch pollen already observed to take place from north and central Europe to Scandinavia (Emberlin, 1994). Transcontinental transport of dust particulates has also been observed. To the extent that climate change increases the frequency of weather events that facilitate such transcontinental transport, it could increase the likelihood of additional aeroallergens being introduced into the United States. Whether long-range transport of pollen may instead decrease aeroallergen concentration and distribution so as to decrease human exposures has not been reported.

The links to allergic diseases

Shifts in phenology (periodic phenomena that are related to climate change) are one of the most consistent findings in studies of plant pollen production. Alterations in the timing of aeroallergen production in response to weather variables have been clearly demonstrated for certain tree species, but less so for grass and weed pollen and mold. Analyses of trends in allergic diseases are based on annual prevalence and generally do not document the seasonal timing of these diseases within the year. In sensitized individuals, however, exposure clearly leads to allergic response; thus, it is reasonable to expect that changes in the timing of production of seasonal aeroallergens would result in corresponding changes in the timing of the associated seasonal allergic diseases. Thus, the National Assessment Synthesis Team (NAST) (Bernard et al., 2001) concluded that climate change may affect the timing or duration of seasonal allergic diseases such as hay fever. However, shifts in the timing of asthma and atopic dermatitis in response to changes in phenology are not well understood.

Increases in aeroallergen production and/or allergen concentration could impact the severity and possibly prevalence of allergic illness via sensitivity and response pathways. On the basis of model projections by the NAST based on climate change scenarios (Melillo et al., 2001), pollen production, and possibly allergen content, in many areas of the country may increase at least through the mid-21st century. Exposures to higher concentrations of allergens may lead to more severe allergic responses (Nielsen et al., 2002). In addition, exposure to elevated pollen and mold concentrations during sensitization may lead to a greater likelihood of development of allergies such as rhinitis. Finally, as noted above, additional aeroallergens might be introduced if

long-range transcontinental transport of pollen and/or mold is facilitated by climate change-induced factors.

Although there is substantial evidence suggesting a causal relationship between aeroallergens and allergic diseases, it remains unclear which aeroallergens are more highly associated with causing sensitization and subsequent disease development. We observe this primarily because of the cross-reactivity of aeroallergens—the ability of two or more aeroallergens with biochemical similarities to elicit an allergic response in an individual who may be sensitized to only one of them. Multiple studies have found cross-reactivity among aeroallergens to be implicated in allergic disease causation.

Not only the type, but also the amount of aeroallergen to which an individual is exposed is influential in the development of an allergic illness. Similar to what is observed in most disease causation scenarios, a dose-response relationship between aeroallergen exposure and sensitization and exacerbation of disease has been observed—i.e., sensitized patients are more likely to have more severe disease if exposure to allergens is high.

There are, thus, at least three causal pathways for climate change-induced impacts on aeroallergens to alter the severity and possibly the prevalence of allergic diseases. First, a longer exposure during sensitization may lead to greater likelihood of the development of allergy. Second, a higher dose during sensitization may lead to a greater likelihood of development of an allergy. Third, a higher dose during subsequent exposures (postsensitization) may lead to a more severe allergic response. For individual patients, we can learn exactly which allergens are responsible for sensitization.

However, as noted earlier, the etiology of allergic diseases, especially asthma, is complex and has a gene-environment interaction that is poorly understood. There are numerous other factors that affect aeroallergen levels and the severity and prevalence of associated allergic diseases, such as changes in land use, air pollution, adaptive responses, and modifying factors; many of which are difficult to assess.

Future research

Further progress must be made in documenting and understanding aeroallergen response to climate, the role of aeroallergens in disease development, and the willingness to pay to avoid the intangible costs of these allergic diseases. A review of the literature indicates there are

limited data on aeroallergen trends in the United States. Integrated long-term data series on all aeroallergens are necessary to clearly document future changes in aeroallergen production and distribution, as well as allergen content. Additional research on the response of mold and indoor allergens to climate change would be of particular value. In addition, further experimental and field studies are needed to examine how allergen content and distribution of aeroallergens may be altered in response to climate change (Beggs, 2004).

There is a need for better understanding of the role of aeroallergens in disease development, especially with respect to asthma. Specifically, what is the relative contribution of different aeroallergens to the development of asthma? There is a need to know what levels of allergen exposure constitute a risk for asthma development. There is also a need for standardized approaches for measuring exposures and outcomes in epidemiologic studies (Selgrade et al., 2006). Finally, the potential synergistic effect of aeroallergens and air pollutants on the development or exacerbation of allergic diseases is an important area for future research.

Based on a review of the cost of illness (COI) literature on allergic rhinitis, asthma, and atopic dermatitis, it is clear that an important research gap is the current lack of assessment of and, in particular, estimation of willingness to pay to avoid the intangible costs of these diseases. In addition, better methodologies are needed to address productivity losses, aeroallergen avoidance, and over-the-counter medication use. Finally, a disease or condition may also contribute to increased costs as a secondary diagnosis, or as a risk factor for other diseases and conditions. These hidden costs of comorbidity need to be properly addressed and, if possible, included in future COI studies.

1. INTRODUCTION

Aeroallergens are classified into three groups: pollens (tree, weed, and grass), molds, and indoor allergens. There is evidence to support a causal relationship between each aeroallergen within these groups and one or more allergic diseases, including allergic rhinitis (hay fever), asthma, and atopic dermatitis (eczema). Over the last 30 years, there has been a substantial increase in the prevalence of allergic diseases within the United States. The prevalence of asthma and allergenic rhinitis has increased from approximately 8–55 per 1,000 persons and approximately 55–90 per 1,000 persons, respectively. The underlying reasons behind the increased prevalence of each illness remain unclear. It has been hypothesized that global climate change could alter the concentrations, distributions, dispersion patterns, and allergenicities of aeroallergens in the environment in ways that could further increase the prevalence of allergic diseases in the United States.

Although climate change projection is still an uncertain science, there have been attempts to derive future climate scenarios, based on projected concentrations of greenhouse gases and models that simulate atmospheric circulation. In 2007, the United Nations Intergovernmental Panel on Climate Change (IPCC) conducted a comprehensive assessment of the science behind projected climate changes. The IPCC report projected changes in average, minimum, and maximum temperature; precipitation patterns; and impacts on cyclical climate patterns, such as the El Niño-Southern Oscillation (ENSO; IPCC, 2007).

The IPCC projects that the average global surface air temperature in the years 2090–2099 is likely to be between 1.8 to 4.0°C warmer than such temperatures in 1980–1999, depending on which climate scenarios are input into the models. Models projecting the global distribution of temperature change project that North America will experience more warming than the average global warming, with the United States projected to have an increase of 2 to 3°C in the western, southern, and eastern areas, with up to 5°C in annual mean temperature by 2100 projected for Alaska (IPCC, 2007). Rising minimum temperatures are expected to result in fewer cold days, frost days, and cold waves globally (IPCC, 2007). Change has already been detected, with global average temperature increasing by more than 0.7°C over the past 100 years, with corresponding increases in the frequency of hot days and decreases in the frequency of cold nights (IPCC, 2007).

Along with increasing temperatures, other effects of climate change, such as changes in precipitation, have also been projected. Globally, precipitation is projected to increase in all areas, with greater certainty for higher latitudes. Projections of precipitation show increases for the northeastern United States, with decreases for the southwest (IPCC, 2007). Present observations indicate that annual land precipitation has increased in the eastern United States (IPCC, 2007).

Overall, heavy precipitation has increased over most land areas, and hurricanes have increased in intensity in the North Atlantic since records began in 1970. The intensity of heavy precipitation events, including hurricanes, is projected to increase, although there is less confidence about projections for their frequency under climate change (IPCC, 2007). Conversely, episodes of drought have occurred more frequently and intensely in recent decades in some regions, particularly the tropics and subtropics (IPCC, 2007).

Overall, the frequency of floods, extreme precipitation events, heat waves, and other extreme weather events have been projected to increase. It is believed that some of the expected changes will be caused by the projected increase in temperature because higher temperatures can affect the hydrological cycle by increasing evaporation and allowing more water vapor to be held in the atmosphere. It remains unclear if the frequency of small-scale weather events such as thunderstorms and tornadoes will change, because there is insufficient information to include these in global models (IPCC, 2007).

ENSO events are cyclical changes in sea surface temperatures and air pressure, and they result in short-term episodes of increased climate variability. El Niño events generally occur in cycles of 3 to 6 years, and there are periods of higher and lower strength of ENSO on larger time scales of decades, causing very different impacts globally (IPCC, 2007). ENSO events are associated with changes in precipitation globally, with some regions becoming wetter during El Niño events (e.g., eastern North America) and other areas getting drier (e.g., western North America). The strong influence of ENSO on tropical monsoons means that any changes in ENSO due to climate change can affect rainfall patterns in many parts of the Pacific region (IPCC, 2007). El Niño events have occurred with greater frequency over the last few decades, with the El Niño event of 1997–1998 being the strongest recorded (Sutherst, 2004). All climate models project that ENSO interannual variability will continue; however, there are many

differences between models about changes to ENSO due to climate change. Additionally, there are other measures of global climate variability (IPCC, 2007).

The potential impacts of these climatic changes on aeroallergens and allergic diseases in the United States are unclear. Current research has focused on examining how specific elements of climate change (e.g., increased CO₂ levels, changing temperatures, and increased and decreased regional precipitation) can alter the production, distribution, and allergen content of aeroallergens. A change in any of these characteristics of aeroallergens could lead to a substantial increase in the overall prevalence of allergic diseases in the United States, above and beyond the increase already observed.

This report provides an overview of the literature detailing the potential impacts of climate change on aeroallergens and their associated allergic diseases in the United States. Section 2 provides background information on the major aeroallergens in the United States and the allergic diseases associated with them. Section 3 outlines historical trends in levels of aeroallergens and the prevalence of their associated allergenic illnesses in the United States. Section 4 discusses the evidence of links between climate variability and aeroallergens in the United States, especially the potential indirect impacts on the allergenic illnesses associated with them and the evidence of links between climate variability and allergic diseases. Section 5 discusses the economic and quality-of-life implications of allergenic diseases on populations in the United States. Finally, Section 6 addresses the current gaps in knowledge about the impacts of climate change on aeroallergens and allergenic illnesses.

2. AEROALLERGENS AND ASSOCIATED ALLERGIC DISEASES IN THE UNITED STATES

2.1. AEROALLERGENS

Aeroallergens are classified into three primary categories: pollen, mold, and indoor allergens. Clinically relevant aeroallergens in North America, identified in *Practice Parameters for Allergen Immunotherapy*, the 2003 publication by the Joint Council of Allergy, Asthma and Immunology (JCAAI), are shown in Table 2-1.

The JCAAI identified the most common aeroallergens through consensus opinion of experts, rather than through evidence derived from clinical studies identifying a causal relationship between aeroallergen exposure and an allergic illness (White et al., 2005). In contrast, White et al. (2005) defined major tree pollen allergens as those aeroallergens in which percutaneous reactivity to a given tree pollen extract resulted in more than 50% of all patients having a positive skin prick test. Using this definition, White et al. (2005) identified American sycamore, American elm, box-elder, red maple, white ash, cottonwood, and black walnut—all included in Table 2-1 above—as “major allergens,” but they did not recognize mulberry, also included in Table 2-1, as a major aeroallergen. As this example shows, the inconsistencies in the definitions of a “major aeroallergen” can result in the identification of clinically relevant aeroallergens not listed in Table 2-1. Other examples include the grass pollen orchard (*Dactylis glomerata*), Kentucky blue grass (*Poa pratensis*), Red top (*Agrostis alba*), and Sweet vernal (*Anthoxanthum odoratum*) (American Academy of Allergy, Asthma & Immunology [AAAAI], 2002). Throughout this report, Table 2-1 will be taken to represent the most common aeroallergens; however, regional differences, future changes in plant populations, and differences in the definition of what constitutes a major aeroallergen could result in the addition of aeroallergens to this list in the future (White and Bernstein, 2003).

2.1.1. Pollen

The major pollen allergens are divided into three subcategories: tree pollen, grass pollen, and weed pollen. The pollen size for all of the subcategories varies from 5 μm to greater than 200 μm (Wood, 1986). The pollen of each species has a distinct distribution, season of pollination, and level of dispersal, as discussed in detail by Kosisky and Carpenter (1997);

Table 2-1. Selection of clinically relevant aeroallergens in the United States

Latin name	Common name
Tree pollen	
<i>Acer negundo</i>	Box-elder
<i>Acer rubra</i>	Red maple
<i>Alnus rubra</i>	Alder
<i>Betula papyrifera</i>	Paper birch
<i>Carya illinoensis</i>	Pecan
<i>Fraxinus Americana</i>	White ash
<i>Juglans nigra</i>	Black walnut
<i>Juniperus ashei</i>	Mountain cedar
<i>Morus alba</i>	Mulberry
<i>Olea europaea</i>	Olive
<i>Plantanus occidentalis</i>	American sycamore
<i>Populus deltoids</i>	Eastern cottonwood
<i>Quercus alba</i>	White oak
<i>Quercus rubra</i>	Red oak
<i>Ulmus Americana</i>	American elm
<i>Ulmus parvifolia</i>	Chinese elm
<i>Ulmus pumila</i>	Siberian elm
Grass pollen	
<i>Cynodon dactylon</i>	Bermuda
<i>Festuca elatior</i>	Meadow fescue
<i>Holcus halepensis</i>	Johnson
<i>Lolium perenne</i>	Rye
<i>Paspalum notatum</i>	Bahia
<i>Phleum pretense</i>	Timothy
Weed pollen	
<i>Amaranthus retroflexus</i>	Red root pigweed
<i>Ambrosia artemisiifolia</i>	Short ragweed
<i>Artemisia vulgaris</i>	Mugwort
<i>Kochia scoparia</i>	Burning bush
<i>Plantago lanceolata</i>	English plantain
<i>Rumex acetosella</i>	Sheep sorrel
<i>Salsola kali</i>	Russian thistle

Table 2-1. Selection of clinically relevant aeroallergens in the United States (continued)

Latin name	Common name
Mold	
<i>Alternaria alternata</i>	N/A
<i>Aspergillus fumigatus</i>	N/A
<i>Cladosporium</i> (<i>C. cladosporioides</i> ; <i>C. herbarum</i>)	N/A
<i>Drechslera</i> or <i>Bipolaris</i> type (e.g., <i>Helminthosporium solani</i>)	N/A
<i>Epicoccum nigrum</i>	N/A
<i>Penicillium</i> (<i>P. chrysogenum</i> ; <i>P. expansum</i>)	N/A
Indoor allergens	
<i>Felis domesticus</i>	Cat (epithelium)
<i>Canis familiaris</i>	Dog (epithelium)
<i>Dermatophagoides farinae</i> ; <i>Dermatophagoides pteronyssinus</i>	House dust mites
<i>Blattella germanica</i>	German cockroach

Source: Joint Task Force on Practice Parameters (2003).

however, within a pollen type (e.g., tree pollen), there are many similarities across species. In a study observing pollen levels during a 5-year period in Washington, D.C., Kosisky and Carpenter (1997) found tree pollen accounts for approximately 90% of the total annual pollen produced, with weeds and grasses accounting for 6 and 3%, respectively. The results reported by Kosisky and Carpenter (1997) are consistent with the results of similar studies observing yearly pollen levels. For example, in a study conducted in Philadelphia and Southern New Jersey, Dvorin et al. (2001) found that tree pollen accounts for the largest percent (approximately 75%) of the total annual pollen produced. Although there are clear differences in the amounts of different types of pollen produced, other factors, including prevailing winds and the pattern of land use, may also affect the level of airborne allergens in an area (Wood, 1986). The following sections discuss the defining characteristics of each pollen type, including the distributions of the relevant plant species within the United States, the pollen seasons, and the levels of pollen dispersal.

2.1.1.1. *Tree Pollen*

Tree pollen accounts for the largest percent of pollen produced during the pollen season—approximately 75 to 90% (Dvorin et al., 2001; Kosisky and Carpenter, 1997). Of the total amount produced, however, only a small percentage is pollen generated from clinically relevant tree species. During a study of 5-year mean tree pollen counts, for example, White et al. (2005) found that “major allergens” accounted for only 5% or less of the total 5-year mean tree pollen count.¹ In a similar study, Kosisky and Carpenter (1997) found oak pollen represented approximately 57% of the pollen produced during a 6-year period in Washington, D.C.; however, there are 20 species of oak in the D.C. area, only two of which (white oak and red oak) produce pollen counted among the major aeroallergens. This suggests that, in the case of Washington, D.C., allergenic tree pollen may represent only a small percentage of the total tree pollen produced on a yearly basis. Nevertheless, a small percentage still represents a large number of persons affected.

Studies conducted by Weber (2003a, b) and White and Bernstein (2003) identified regions of the major tree pollen allergens in the United States by hardiness zones (i.e., climatic zones) defined by the United States Department of Agriculture (Weber, 2003a, b). White and Bernstein (2003) went a step farther and defined geographic locations for each pollen type through the designation of east or west, with the dividing line between east and west, running from the middle of Montana diagonally to just east of the southern tip of Texas. One or more U.S. Census Bureau geographic regions (e.g., Midwest [MW], Northeast [NE], South [S], and West [W]) was assigned to each tree pollen type based on the tree growth region data provided in Weber (2003a, b), and White and Bernstein (2003) and National Center for Health Statistics, (2004) (Table 2-2). Overall, the distribution of tree pollen spans the entire United States, but the abundance of pollen produced by certain tree species can vary within their defined geographic region(s).

¹White et al. (2005) identified American sycamore, American elm, box-elder, red maple, red oak, white ash, cottonwood, and black walnut as “major allergens.” They did not classify mulberry as a major allergen; therefore, it is possible that the total percent contribution of “major allergens” to the 5-year mean tree pollen count could be slightly larger than 5%.

Table 2-2. Geographic distribution of major clinically relevant tree pollen in the United States

Latin name	Common name	Geographic region(s) ^a
<i>Acer negundo</i>	Box-elder	MW, NE, S, W
<i>Acer rubra</i>	Red maple	MW, NE, S
<i>Alnus rubra</i>	Alder	W
<i>Betula papyrifera</i>	Paper birch	MW, NE, W
<i>Carya illinoensis</i>	Pecan	MW, S
<i>Fraxinus americana</i>	White ash	MW, NE, S
<i>Juglans nigra</i>	Black walnut	MW, NE, S
<i>Juniperus ashei</i>	Mountain cedar	AR, MO, OK, TX ^b
<i>Morus alba</i>	Mulberry	MW, NE, S
<i>Olea europaea</i>	Olive	W ^c
<i>Plantanus occidentalis</i>	American sycamore	MW, NE, S
<i>Populus deltoids</i>	Eastern cottonwood	NE, S
<i>Quercus alba</i>	White oak	MW, NE, S
<i>Quercus rubra</i>	Red oak	MW, NE, S
<i>Ulmus Americana</i>	American elm	MW, NE, S
<i>Ulmus parvifolia</i>	Chinese elm	MW, NE, S, W
<i>Ulmus pumila</i>	Siberian elm	MW, NE, S, W

^a MW = Midwest; NE = Northeast; S = South; W = West.

^bMountain cedar is located throughout the United States but is highly prevalent in central Texas and other areas of the southern Great Plains (Levetin and Van de Water, 2003).

^cOlive is most prevalent in the Southwest United States (White and Bernstein, 2003).

Sources: Weber (2003a, b), White and Bernstein (2003).

The pollen seasons of the clinically relevant tree species are shown in Table 2-3. The overall pollen season for tree pollen tends to last from early March to mid-May; although in some cases, it can run from February to June (Kosisky and Carpenter, 1997; White et al., 2005). The one exception to this is the unique pollen season of Mountain Cedar (*Juniperus ashei*), which ranges from December to January (Levetin and Van de Water, 2003).

The period from late April to early May is of particular importance because this is the period with the highest pollen prevalence due to considerable overlap of the pollen seasons of multiple tree species (Dvorin et al., 2001). April, in particular, has been found to have the highest weekly average pollen concentrations (Kosisky and Carpenter, 1997). During the pollen

season, multiple tree species will release pollen at the same time, resulting in a significant amount of pollen being dispersed. The release of pollen from these tree species and, subsequently, all tree species during the pollen season can result in the weekly average pollen concentration per tree exceeding 100 grains/m³, with the cumulative pollen abundance over the pollen season for each tree ranging upwards of 1,800 grains/m³ (Dvorin et al., 2001).

Table 2-3. Pollen seasons of the major clinically relevant tree pollen in the United States

Latin name	Common name	Pollen season	Reference
<i>Acer negundo</i>	Box-elder	Early spring	Phadia, 2002
<i>Acer rubra</i>	Red maple	Mid-April to Mid-May	Dvorin et al., 2001
<i>Alnus rubra</i>	Alder	February to April	Weber, 2003a, b
<i>Betula papyrifera</i>	Paper birch	Late April to Late May	Dvorin et al., 2001
<i>Carya illinoensis</i>	Pecan	April to June	Phadia, 2002
<i>Fraxinus americana</i>	White ash	April to May	Phadia, 2002
<i>Juglans nigra</i>	Black walnut	Late spring (May) to Early summer	Levetin, 2006; Phadia, 2002
<i>Juniperus ashei</i>	Mountain cedar	December to January	Levetin and Van de Water, 2003
<i>Morus alba</i>	Mulberry	Spring; April to May	Levetin, 2006; Phadia, 2002
<i>Olea europaea</i>	Olive	Spring	Phadia, 2002
<i>Plantanus occidentalis</i>	American sycamore	March to April	Levetin, 2006
<i>Populus deltoids</i>	Eastern cottonwood	March to April	Levetin, 2006
<i>Quercus alba</i>	White oak	March to May	Dvorin et al., 2001; Levetin, 2006
<i>Quercus rubra</i>	Red oak	March to April	Levetin, 2006
<i>Ulmus Americana</i>	American elm	February to March ^a	Levetin, 2006
<i>Ulmus parvifolia</i>	Chinese elm	Fall	Tidwell, 2006
<i>Ulmus pumila</i>	Siberian elm	February to March ^a	Tidwell, 2006

^aPollen season can possibly extend to April (Saint Louis County, 2006).

2.1.1.2. Grass Pollen

Grass pollen accounts for the smallest percent of pollen produced during the pollen season—approximately 3 to 10% (Dvorin et al., 2001; Kosisky and Carpenter, 1997). The literature does not address what percentage of the total grass pollen count is composed of the clinically relevant grass pollen, however, as it does for tree pollen; therefore, the total amount of clinically-relevant grass pollen produced on a yearly basis is not well-defined.

As for tree pollen, the distributions of grass pollen within the United States were determined using data detailed in Weber (2003a, b) and White and Bernstein (2003), and then extrapolated to the United States regions defined by the U.S. Census Bureau. Table 2-4 shows the geographic regions of the most common clinically relevant grass pollen in the United States. Consistent with what has been reported for tree pollen, the distribution of grass pollen can vary considerably within defined geographic region(s). Grass pollen is usually deposited within 50 miles of its release, and although the exact distance can vary, it will mostly be confined to the relative vicinity in which it grows (Wood, 1986).

Table 2-4. Geographic distribution of major clinically relevant grass pollen in the United States

Latin name	Common name	Geographic region(s)^a
<i>Cynodon dactylon</i>	Bermuda	MW, S, W ^b
<i>Festuca elatior</i>	Meadow fescue	MW, NE, S, W ^c
<i>Holcus halepensis</i>	Johnson	MW, S, W ^{b,d}
<i>Lolium perenne</i>	Rye	MW, NE, S, W ^c
<i>Paspalum notatum</i>	Bahia	MW, S, W ^b
<i>Phleum pretense</i>	Timothy	MW, NE, S, W ^c

^a MW = Midwest; NE = Northeast; S = South; W = West.

^bBermuda, Johnson, and bahia are all located in the southern part of each region from the East to the West coast of the United States and are becoming increasingly more important in the south (Phipatanakul, 2005; White and Bernstein, 2003).

^cMeadow fescue, Rye, and Timothy are all located in the northern part of each region from the East to the West coast of the United States (White and Bernstein, 2003).

^dThe growing region of Johnson extends slightly further north than that of Bermuda and bahia (White and Bernstein, 2003).

Sources: Weber (2003a, b), White and Bernstein (2003).

Unlike tree pollen, some grass pollen, including Bermuda, Johnson, and Bahia, are produced all year (Weber, 2003a, b). Dvorin et al. (2001) found that for the majority of grasses, the pollen season tends to last from late April to mid-June, with a secondary peak in early September. These findings are consistent with what has been defined as the peak grass pollen season, from May through June (Gonzalez Minero et al., 1998). Table 2-5 shows the pollen season for each of the clinically relevant grass pollens.

During the peak months of the grass pollen season, the cumulative weekly average concentration of pollen is typically >100 grains/m³, with the cumulative amount of pollen produced in a single year not exceeding 2,500 grains/m³ (Gonzalez Minero et al., 1998). During the pollen season, grass pollen levels can oscillate both during the season and throughout a region due to anthropogenic factors. The levels can vary depending on the amount of land covered in grass; the seed mix of sown pastures, and the replacement of haymaking by silage production, when grasses are cut before they flower (Nielsen et al., 2002).

Table 2-5. Pollen season of the major clinically relevant grass pollen in the United States

Latin name	Common name	Pollen season
<i>Cynodon dactylon</i>	Bermuda	Late April to mid-June, early September
<i>Festuca elatior</i>	Meadow fescue	Late April to mid-June, early September
<i>Holcus halepensis</i>	Johnson	Late April to mid-June, early September
<i>Lolium perenne</i>	Rye	Late April to mid-June, early September
<i>Paspalum notatum</i>	Bahia	Late April to mid-June, early September
<i>Phleum pratense</i>	Timothy	Late April to mid-June, early September

2.1.1.3. Weed Pollen

Weed pollen accounts for the second greatest percentage of pollen produced during the pollen season—approximately 6 to 17%. However, the amount produced is significantly less than the total amount of tree pollen produced in a single year (Dvorin et al., 2001; Kosisky and Carpenter, 1997). Similar to grass pollen, the literature for weed pollen does not address what percentage of the total weed pollen count is composed of the clinically relevant weed pollen; therefore, the total amount of clinically relevant weed pollen produced on a yearly basis is not clearly defined.

As for both tree and grass pollen, the distribution of weed pollen within the United States was determined using data detailed in Weber (2003a, b) and White and Bernstein (2003), and then extrapolated to the United States regions defined by the U.S. Census Bureau.

Table 2-6 details the geographic regions of the most common weed pollen in the United States. Although all of the major weeds are located throughout the United States, some are more highly prevalent in specific regions of the country.

Table 2-6. Geographic distribution of major clinically relevant weed pollen in the United States

Latin name	Common name	Geographic region(s) ^a
<i>Amaranthus retroflexus</i>	Red root pigweed	MW, NE, S, W ^b
<i>Ambrosia artemisiifolia</i>	Short ragweed ^c	MW, NE, S, W ^d
<i>Artemisia vulgaris</i>	Mugwort	MW, NE, S, W ^e
<i>Kochia scoparia</i>	Burning bush	MW, NE, S, W
<i>Plantago lanceolata</i>	English plantain	MW, NE, S, W
<i>Rumex acetosella</i>	Sheep sorrel	MW, NE, S, W ^b
<i>Salsola kali</i>	Russian thistle	MW, NE, S, W ^b

^a MW = Midwest; NE = Northeast; S = South; W = West.

^b Found throughout the United States, but especially in the western half of the United States (Powell and Smith, 1978; White and Bernstein, 2003).

^c Not found in the Pacific Northwest (Phipatanakul, 2005).

^d Not found in Utah, Nevada, and California (White and Bernstein, 2003).

^e Highly localized to the eastern United States and Pacific Northwest (White and Bernstein, 2003).

Sources: Weber (2003a, b), White and Bernstein (2003).

Unlike the tree and grass pollen seasons, which are relatively consistent across all species, the pollen season for weeds has been shown in multiple studies to vary across species (Table 2-7). In some cases, the region of the country in which the weed species is located can influence the pollen season. For example, in most areas of North America, ragweed pollinates from August through October, but the pollen season tends to be earlier in northern areas and progressively later in southern states (Levetin and Van de Water, 2003). Overall, the weed pollen season is typically defined as mid-August through late-September (Dvorin et al., 2001).

Table 2-7. Pollen season of the major clinically relevant weed pollen in the United States

Latin name	Common name	Pollen season	Reference
<i>Amaranthus retroflexus</i>	Red root pigweed	Late Summer and Autumn	Phadia, 2002
<i>Ambrosia artemisiifolia</i>	Short ragweed	March to November ^a	Weber, 2003a, b
<i>Artemisia vulgaris</i>	Mugwort	August to October	White and Bernstein, 2003
<i>Kochia scoparia</i>	Burning bush	Mid-Summer	Phadia, 2002
<i>Plantago lanceolata</i>	English Plantain	July to August ^b	Weber, 2003a, b
<i>Rumex acetosella</i>	Sheep sorrel	April to May ^c ; Mid-August to Late September	Dvorin et al., 2001; Weber, 2003a, b
<i>Salsola kali</i>	Russian thistle	Late Summer and Autumn	Phadia, 2002; Powell and Smith, 1978

^aPollen season is August to October in northern regions of the United States (Dvorin et al., 2001; White and Bernstein, 2003).

^bPollen season may extend slightly longer, May to October, with the peak being May to July (White and Bernstein, 2003).

^cSpecific to western United States.

During the peak pollen season, from mid-August through late-September, weed pollen levels may exceed 250 grains/m³ weekly (Dvorin et al., 2001). The total amount of pollen released during the pollen season can vary from region to region, with the total amount of pollen released being determined by the prevalence of each weed species in each geographic region of the United States. For example, although it is found throughout the United States, ragweed has high pollen counts in the Omaha region of the Midwest, which will highly influence the overall weed pollen count in that region of the country (Weber, 2003a, b).

2.1.2. Mold

The second major class of clinically relevant aeroallergens is mold. Mold spores are substantially smaller than pollen grains, ranging in size from 2 to 10 µm, and are more abundant (Burge, 2002). Mold counts are often 1,000-fold greater than pollen counts (Bush and Prochnau,

2004).² Unlike pollen, mold is not localized to specific regions of the country; it can be found throughout the United States, except in the coldest regions, but it can be found in higher concentrations in some regions due to specific environmental conditions, most notably humidity (Phipatanakul, 2005) (Table 2-8). Mold requires a consistently high relative humidity, ranging between 70 and 85% (Burge, 2002; Hamilton and Eggleston, 1997).

Table 2-8. Geographic distribution of major clinically relevant mold in the United States

Latin name	Geographic region ^a	Reference
<i>Alternaria alternata</i>	Grain-growing areas	Corden and Millington, 2001; Targonski et al., 1995
<i>Aspergillus fumigatus</i>	Warm climates (>40°C)	Hamilton and Eggleston, 1997
<i>Cladosporium</i> (<i>C. cladosporioides</i> ; <i>C. herbarum</i>)	Temperate zones	Hamilton and Eggleston, 1997
<i>Drechslera</i> or <i>Bipolaris</i> type (e.g., <i>Helminthosporium solani</i>)	N/A	N/A
<i>Epicoccum nigrum</i>	N/A	N/A
<i>Penicillium</i> (<i>P. chrysogenum</i> ; <i>P. expansum</i>)	N/A	N/A

^aStudies detailing common mold aeroallergens do not address their distribution within the United States. The literature has hinted at mold being found ubiquitously in the United States. Areas or regions of the United States are included for those types of mold where information was available.

Mold is primarily located outdoors, but unlike pollen, can colonize indoor materials (Burge, 2002). *Alternaria* and *Cladosporium* are universally dominant outdoor fungal species that are detected indoors, while *Penicillium* and *Aspergillus* are universally dominant indoors (Hamilton, 2005). Burge et al. (2002) found that the concentrations of outdoor fungal species in indoor environments are driven by outdoor concentrations. Indoors, the distribution of fungal concentrations throughout the aboveground living space of a home is fairly consistent, with the highest concentrations being found in basements due to ideal growing conditions, but the types found in basements are usually not related to those found outdoors (Burge, 2002).

²Hamilton and Eggleston (1997) state, although fungal counts are substantially larger than those observed for pollen, it is currently unclear if the viable spore colony count or the total (viable and nonviable) spore count is a better indicator for clinically relevant mold allergens in the environment.

The literature focuses primarily on *Alternaria*, one of the more common atmospheric mold spores in the United States (Corden and Millington, 2001). *Alternaria* flourishes in warm, humid environments (Hamilton and Eggleston, 1997). It grows well on fruits and tomatoes, as well as textiles, allowing it to flourish in indoor environments; however, it is usually not found indoors (Corden and Millington, 2001; Hamilton and Eggleston, 1997). *Alternaria* is found in highest concentrations in cultivated areas, such as the Midwest, in which grasslands and grain fields predominate (Bush and Prochnau, 2004). In studies conducted in Derby, UK by Corden and Millington (2001), and in Chicago by Targonski et al. (1995), seasonal *Alternaria* concentrations were observed primarily from June to October, and July to October, respectively, periods which coincide with harvest time, although spores were occasionally found at other times throughout the year. *Cladosporium* is the most abundant mold spore in temperate parts of the world. *Alternaria* counts are 10 to 100 times lower than *Cladosporium*.

Unfortunately, information for the other clinically relevant molds is limited. Specific regions of growth and periods of highest concentration have been identified for only a few mold types, as shown in Table 2-8. *Cladosporium* thrives in temperate zones, and *Aspergillus* thrives in warm climates (>40°C), while *Penicillium* grows on stale bread, citrus fruits, and apples (Hamilton and Eggleston, 1997). It is unclear if a specific time of year is associated with increased concentrations of *Cladosporium* and *Penicillium*, but *Aspergillus* concentrations do have seasonal peaks, provided they penetrate indoor environments when heating is the highest, during autumn and winter (Hamilton and Eggleston, 1997).

There are many other fungal species that have been studied for allergenicity,³ including molds, mushrooms, and yeasts; however, few of the fungal allergens have been well-characterized, possibly due to the complexity and large number of fungal spores (Horner et al., 1995). Thus, this report limits itself to the well-studied mold allergens, noting that there may be many more important fungal allergens discovered in the future.

2.1.3. Indoor Allergens

Similar to mold, indoor allergens are not particularly associated with specific regions of the United States. Indoor environments have been found to be the main determinant influencing the level of indoor allergens. It has been postulated that an increase in the price of energy has

³Allergenicity refers to the degree to which a protein is likely to elicit an allergic response. However, the term is periodically used in the literature in reference to pollen protein concentrations.

resulted in an increase in insulation and a decrease in ventilation in buildings, providing ideal growth conditions for the most prevalent indoor allergen, house dust mites (Nielsen et al., 2002). House dust mites are ubiquitous throughout the United States except in very dry climates and at higher elevations (Phipatanakul, 2005). They have also been found to thrive in warm conditions where the relative humidity is approximately 70% (Hamilton, 2005). Cockroaches, on the other hand, are found more predominantly in urban areas, particularly in inner city, low-income environments, but are also more common than previously thought in suburban middle-class homes (Hamilton, 2005; Phipatanakul, 2005). The concentrations of all indoor allergens do not vary with season as is observed for pollen and some mold, but are instead found perennially. Indoor allergens are not confined to specific regions of the United States, but factors have been identified that influence the level of allergens found indoors. Major clinically relevant indoor allergens include cat epithelium, dog epithelium, domestic mites, and German cockroaches (Table 2-9).

Table 2-9. Geographic distribution of major clinically relevant indoor allergens

Latin Name	Common name	Geographic region(s)^a
<i>Penicillium</i>	Penicillium mold	N/A
<i>Felis domesticus</i>	Cat (epithelium)	N/A
<i>Canis familiaris</i>	Dog (epithelium)	N/A
<i>Dermatophagoides farinae</i> ; <i>Dermatophagoides pteronyssinus</i>	Dust mites	N/A
<i>Blattella germanica</i>	German cockroach	N/A

^aIndoor allergens are not confined to specific regions of the United States, but factors have been identified that influence the levels of allergens found indoors.

2.2. ASSOCIATED ALLERGIC DISEASES

Exposure to allergens results in allergic diseases in approximately 20% of the United States population (AAAAI, 1996–2006). The development of allergic diseases occurs through a two-stage process. In the first stage, an immunologically naïve individual is sensitized to an allergen, resulting in the production of IgE antibodies. In the second stage, renewed exposure to the allergen elicits a disease response due to the presence of IgE antibodies and the associated cellular response (Nielsen et al., 2002). Currently, three main allergic diseases have been

associated with exposure to aeroallergens: allergic rhinitis (hay fever), asthma, and atopic dermatitis (eczema).

The initial sensitization to an aeroallergen can occur during any period of an individual's life. Wood (1986) cites a study by Ziering and Klein (1982), which found that respiratory allergies develop by 2 years of age in 40% of those affected and by 6 years of age in the remaining 60%. Wood (1986) also cites a study by Kemp (1979) that found that the sensitivity to grass pollen of children who reached the age of 3 months during a time of high environmental exposure to grass pollen was significantly greater than the sensitivity to grass pollen of children born at other times of the year. Although sensitization and the subsequent development of allergic diseases can occur during childhood, sensitization to common aeroallergens increases with age and with the length of the exposure period (Nielsen et al., 2002). The German Multicenter Allergy birth cohort study, for example, observed rates of sensitization to grass pollen and dust mites of 6.2 and 3.0%, respectively, before the age of 2, but as the children grew older, the rates of sensitization to both outdoor and indoor allergens increased (Phipatanakul, 2005). The incidence of allergic rhinitis was observed in the study to increase by as much as 3 to 4% each year after the age of three (Phipatanakul, 2005).

Underlying genetic factors have been found to have a strong influence on the process of sensitization and the subsequent development of allergic diseases during the course of an individual's life. Individuals classified as atopic (a probably hereditary allergy) are inheritably predisposed to produce elevated amounts of IgE antibodies upon exposure to allergens, and as a result, are more easily sensitized to allergens than are nonatopic individuals (Nielsen et al., 2002). The hereditary association between aeroallergen exposure and allergic illness development has been identified as a primary risk factor for the development of allergic rhinitis in children, especially if both parents are affected by the illness (Phipatanakul, 2005). Although there is a major hereditary contribution to the development of these allergic diseases, environmental factors, specifically exposure to aeroallergens, play a significant role in their manifestation (Nielsen et al., 2002).

The degree to which an aeroallergen causes an allergic illness in a sensitized individual depends on multiple factors, one of the primary factors being the aeroallergen to which the individual is exposed. Galant et al. (1998) performed skin prick tests for different allergens on individuals in California with allergic rhinitis and asthma and found that some allergens are more

prone to result in the development of allergic diseases than others. The study showed the following rank order of positive responses: pollen (grasses > weeds > trees) and house dust mites > pets (cat > dog) > cockroach and mold (Galant et al., 1998). These findings are consistent with the findings in other studies that have examined the association between aeroallergen exposure and the development of allergic diseases. For example, Nielsen et al. (2002) reported that allergy to mold alone has low projective value for the development of asthma and allergic rhinitis. In one study, 15% of subjects sensitized exclusively to mold had allergic symptoms, but subjects sensitized to mold and pollen and/or house dust mites had a prevalence of allergic symptoms of about 50%, suggesting that sensitization to mold alone is not as important in causing allergic symptoms as sensitization to the other aeroallergens (Nielsen et al., 2002). In addition, a study conducted in central Indiana found the sensitization rate to mold was only about half the sensitization rate for pollen (Nielsen et al., 2002).

Not only the type, but also the amount of aeroallergen to which an individual is exposed is influential in the development of an allergic illness. Similar to what is observed in most disease causation scenarios, a dose-response relationship between aeroallergen exposure and sensitization and exacerbation of disease has been observed—i.e., sensitized patients are more likely to have more severe disease if exposure to allergens is high (Nielsen et al., 2002). This relationship was observed in a study conducted in France, which looked at hay fever and grass pollen sensitivity. The study found the prevalence of allergy to a given allergen is higher in communities that are heavily exposed to allergens than those that are not (Burr, 1999). Although the probability of an allergic response increases with increasing levels of exposure to aeroallergens, a large exposure is not required to initiate allergic symptoms. Comtois and Gagnon (1988) found that it only takes a small amount, 9 to 23 grains/m³ of tree pollen and 4 to 12 grains/m³ of grass pollen, to cause allergic symptoms in an already-sensitized individual.

The observation of a dose-response relationship between aeroallergen exposure and the development of allergic illness is not specific to pollen exposure; such dose-response relationships have also been observed for individuals sensitized to indoor allergens, specifically house dust mites. Nielsen et al. (2002) found the level of indoor allergen exposure highly influenced the severity of asthma. Because of this, exposure reduction is one of the main methods used to control the development of allergic illness in sensitized individuals (Nielsen et al., 2002).

Although there may be a dose-response relationship between aeroallergen exposure and the development of allergic illness, other confounding factors may make this relationship difficult to observe. If, for example, the proportion of the population that is genetically predisposed to develop allergic diseases happens to decrease as the level of the aeroallergen increases, a dose-response relationship could be masked. Although multiple studies have shown a correlation between aeroallergen levels and disease development, this is not the case for all such studies. White et al. (2005) found no association between regional pollen levels and the frequency of skin test reactivity to specific tree pollen allergens in a study conducted in Southwestern Ohio. These researchers noted that their findings might be specific to Southwestern Ohio; however, these findings call into question whether increased exposure to aeroallergens elicits the same disease response throughout the United States.

All of the factors discussed above influence the development of allergic diseases in individuals exposed to aeroallergens. Table 2-10 shows the allergic diseases associated with exposure to each of the clinically relevant aeroallergens listed in Table 2-1.⁴ The allergic diseases associated with exposure to aeroallergens are discussed more fully below, including the evidence supporting causal relationships between aeroallergen exposure and disease development.

2.2.1. Allergic Rhinitis

The most common allergic illness associated with exposure to aeroallergens is allergic rhinitis (hay fever). Allergic rhinitis is also commonly referred to as rhinoconjunctivitis—because the clinical manifestations associated with the condition may include not only sneezing, itching rhinorrhea, or nasal congestion, but, also, itchy, red, and watery eyes (conjunctivitis) (Phipatanakul, 2005). It is also sometimes called pollinosis, because seasonal allergic rhinitis is primarily caused by airborne pollen (Nielsen et al., 2002). In some cases, the symptoms of allergic rhinitis may also affect the ears and throat and include postnasal drainage (Phipatanakul, 2005). All of these symptoms result from exposure to aeroallergens after an initial sensitization; hence allergic rhinitis is termed a type 1 or immediate hypersensitivity reaction (Wood, 1986).

⁴Table 2-10 does not include atopic dermatitis (eczema) because the literature to date has not definitively concluded that there is a casual association between aeroallergen exposure and atopic dermatitis development (Whitmore et al., 1996).

Table 2-10. Allergic diseases correlated with the major clinically relevant aeroallergens

Latin name	Common name	Allergic illness	Reference
Tree pollen			
<i>Acer negundo</i>	Box-elder	Asthma, Allergic rhinitis	Phadia, 2002; White et al., 2005
<i>Acer rubra</i>	Red maple	Allergic rhinitis	White et al., 2005
<i>Alnus rubra</i>	Alder	Allergic rhinitis ^a	Nielsen et al., 2002
<i>Betula papyrifera</i>	Paper birch	Asthma, Allergic rhinitis	White et al., 2005; White and Bernstein, 2003; Emberlin et al., 2002
<i>Carya illinoensis</i>	Pecan	Allergic rhinitis ^{a, d}	White et al., 2005
<i>Fraxinus americana</i>	White ash	Asthma, Allergic rhinitis	Phadia, 2002; White et al., 2005
<i>Juglans nigra</i>	Black walnut	Allergic rhinitis	White et al., 2005
<i>Juniperus ashei</i>	Mountain cedar	Asthma, Allergic rhinitis	Phadia, 2002
<i>Morus alba</i>	Mulberry	Asthma, Allergic rhinitis	Phadia, 2002
<i>Olea europaea</i>	Olive	Asthma, Allergic rhinitis	Phadia, 2002
<i>Plantanus occidentalis</i>	American sycamore	Asthma, Allergic rhinitis	White et al., 2005; White and Bernstein, 2003
<i>Populus deltoids</i>	Eastern cottonwood	Asthma, Allergic rhinitis	Phadia, 2002; White et al., 2005
<i>Quercus alba</i>	White oak	Allergic rhinitis	White et al., 2005; White and Bernstein, 2003
<i>Quercus rubra</i>	Red oak	Allergic rhinitis	White et al., 2005; White and Bernstein, 2003
<i>Ulmus Americana</i>	American elm	Asthma, Allergic rhinitis	Phadia, 2002
<i>Ulmus parvifolia</i>	Chinese elm	Allergic rhinitis ^a	Nielsen et al., 2002
<i>Ulmus pumila</i>	Siberian elm	Allergic rhinitis ^a	Nielsen et al., 2002
Grass pollen^a			
<i>Cynodon dactylon</i>	Bermuda	Asthma, Allergic rhinitis	Nielsen et al., 2002
<i>Festuca elatior</i>	Meadow fescue	Asthma, Allergic rhinitis	Nielsen et al., 2002
<i>Holcus halepensis</i>	Johnson	Asthma, Allergic rhinitis	Nielsen et al., 2002
<i>Lolium perenne</i>	Rye	Asthma, Allergic rhinitis	Nielsen et al., 2002
<i>Paspalum notatum</i>	Bahia	Asthma, Allergic rhinitis	Nielsen et al., 2002
<i>Phleum pratense</i>	Timothy	Asthma, Allergic rhinitis	Nielsen et al., 2002

Table 2-10. Allergic diseases correlated with the major clinically relevant aeroallergens (continued)

Latin name	Common name	Allergic illness	Reference
Weed pollen			
<i>Amaranthus retroflexus</i>	Red root pigweed	Asthma, Allergic rhinitis	Phadia, 2002
<i>Ambrosia artemisiifolia</i>	Short ragweed	Allergic rhinitis	White and Bernstein, 2003
<i>Artemisia vulgaris</i>	Mugwort	Asthma, Allergic rhinitis	Phadia, 2002
<i>Kochia scoparia</i>	Burning bush	Asthma, Allergic rhinitis	Phadia, 2002
<i>Plantago lanceolata</i>	English plantain	Asthma, Allergic rhinitis	Phadia, 2002
<i>Rumex acetosella</i>	Sheep sorrel	Allergic rhinitis ^a	Nielsen et al., 2002
<i>Salsola kali</i>	Russian thistle	Allergic rhinitis ^a	Nielsen et al., 2002
Mold			
<i>Alternaria alternata</i>	N/A	Asthma, Allergic ^c	Halonen et al., 1997; Corden and Millington, 2001; Andersson et al., 2003
<i>Aspergillus fumigatus</i>	N/A	Asthma	Nielsen et al., 2002
<i>Cladosporium</i> (<i>C. cladosporioides</i> ; <i>C. herbarum</i>)	N/A	Asthma	Nielsen et al., 2002
<i>Drechslera</i> or <i>Bipolaris</i> type (e.g., <i>Helminthosporium solani</i>)	N/A	Asthma ^b	Nielsen et al., 2002
<i>Epicoccum nigrum</i>	N/A	Asthma ^b	Nielsen et al., 2002
<i>Penicillium</i> (<i>P. chrysogenum</i> ; <i>P. expansum</i>)	N/A	Asthma ^b	Nielsen et al., 2002

^aThe literature did not detail a specific allergic illness or diseases associated with exposure to these pollen types. Exposure to all pollen types is known to cause pollinosis (i.e., allergic rhinitis); therefore, allergic rhinitis was listed as the associated allergic illness for these pollen types (Nielsen et al., 2002).

^bThe literature did not detail a specific allergic illness(es) associated with exposure to these types of mold. Nielson et al. (2002) states exposure to mold is a primary risk factor for the development of asthma; as a result, asthma was defined as the associated allergic illness for these types of mold.

^cMold can cause both asthma and allergic rhinitis (Nielsen et al., 2002). Allergic rhinitis is only associated with exposure to *Alternaria* in this table because the literature did not provide definitive evidence that the other types of mold detailed in the table can also cause allergic rhinitis.

^dThe literature does not associate a specific allergic illness with exposure to pecan. It only states pecan is highly allergic (White et al., 2005).

Allergic rhinitis annually affects approximately 20 to 40 million people in the United States, including 10 to 30% of adults and up to 40% of children (Gilmour et al., 2006; O'Connell, 2004). Although exposure to the majority of aeroallergens can result in the development of allergic rhinitis (Table 2-10), sensitization to pollen is a primary risk factor for its development (Nielsen et al., 2002). Pollen from wind-pollinated plants are of particular concern because they are lighter and can become airborne without difficulty, allowing for individuals to be easily exposed (Wood, 1986; White et al., 2005). The significance of pollen exposure in the development of allergic rhinitis was highlighted in a study conducted by the Spanish Society of Clinical Allergy and Immunology. The study found that 65% of pollinosis cases reported in city hospitals were caused by grass pollen (Gonzalez Minero et al., 1998).

Numerous studies have found that exposure to specific pollen types increases the risk of developing allergic rhinitis, but it remains unclear which pollen types are more highly associated with the development of allergic rhinitis. It has been estimated that ragweed pollen is responsible for 50 to 75% of all allergic rhinitis cases in the United States (American College of Allergy, 2006; Nielsen et al., 2002), while 20 to 25% of hay fever sufferers are allergic to birch (Emberlin et al., 2002). A study conducted in Tucson, Arizona, however, found that children who had immediate skin test responses to Bermuda grass were more prone to develop allergic rhinitis (Halonen et al., 1997). These findings are consistent with those of Levetin and Van de Water (2003), who classify Bermuda, Johnson, and bahia as important allergic grasses, but they also contribute to the puzzle about which plant species has the largest influence on the development of allergic rhinitis.

The literature on the development of allergic rhinitis in response to aeroallergen exposure focuses primarily on pollen, but studies have found that exposure to both indoor allergens and mold can also contribute to the development of allergic rhinitis in sensitized individuals. Multiple studies have shown a causal relationship between sensitization for hay fever and exposure to indoor allergens, such as dust mites and cockroaches, as well as exposure to mold. Although exposures to indoor allergens and pollen both result in the development of allergic rhinitis, a difference has been observed in the symptom pattern. Unlike allergic rhinitis symptoms associated with exposure to pollen, which follow the months of the pollen season, the symptoms associated with exposure to indoor allergens are perennial (Phipatanakul, 2005).

The (minimal) literature on the development of allergic rhinitis associated with exposure to mold focuses specifically on *Alternaria*. It has been hypothesized that the smaller spores of

Alternaria (2 to 8 µm) would result in a more potent cause of allergic rhinitis than other types of mold, such as *Cladosporium*, which has much larger spores (Andersson et al., 2003). In a study examining the association between exposure to *Alternaria* in sensitized children and the development of allergic rhinitis, Andersson et al. (2003) concluded that sensitized individuals in regions of the United States with high concentrations of fungal spores are at risk of developing allergic rhinitis.

2.2.2. Asthma

Second only to allergic rhinitis in prevalence, asthma is one of the primary allergic diseases associated with exposure to aeroallergens. Unlike allergic rhinitis, which is primarily associated with exposure to pollen, asthma has been found to be more strongly associated with exposure to indoor allergens and mold. The Centers for Disease Control and Prevention (CDC) estimated the prevalence of asthma in the United States adult population as of 2004 to be 7.5%, or 16 million people, with the overall prevalence in the entire population ranging from 5 to 8% (Gilmour et al., 2006; O'Connell, 2004). It is unclear, however, what percent of the asthma cases identified each year can be attributed solely to exposure to aeroallergens. In epidemiological studies, the proportion of asthmatics who showed an allergic reaction in a skin prick test to one or more common aeroallergens was usually less than one half (Nielsen et al., 2002). Therefore, the estimated prevalence of asthma within the United States may not accurately reflect the prevalence of asthma attributed specifically to exposure to aeroallergens.

Although there is a perceived association between exposure to pollen and asthma development (Table 2-10), pollen exposure has been historically considered to lead primarily to hay fever (Burge, 2002). However, recent data suggest a supporting role for exposure to pollen in the development of asthma (Burge, 2002). In a prospective study conducted in England, detailed by Burr (1999), most patients with grass pollen sensitivity and a history of seasonal exacerbations experienced an asthma attack following a rise in pollen count. White and Bernstein (2003) also found that sensitization to plant aeroallergens is associated with significant morbidity caused by symptoms of seasonal asthma. Although there is mounting evidence that suggests that exposure to pollen can lead to asthma, overall sensitization to pollen remains a low risk factor for asthma development (Nielsen et al., 2002).

The majority of studies examining the development of asthma in response to aeroallergen exposure have focused on the role of indoor allergens and mold. This is primarily because mold, allergens from pets, and cockroaches have shown strong associations with asthma development,

unlike common tree, weed, and grass pollen, which have not shown strong independent associations (Halonen et al., 1997; Nielsen et al., 2002; Hamilton, 2005; Henderson et al., 2000). As with exposure to all aeroallergens, including indoor allergens, sensitization influences the allergic illness an individual will develop. For example, an increased risk of asthma sensitization in atopic individuals has been associated with house dust mite levels higher than 2000 ng/G of fine dust (Hamilton, 2005). After sensitization, exposure to house dust mite levels higher than 10,000 ng/G has been associated with an increased risk of asthma symptoms (Hamilton, 2005). The association between high indoor allergen levels and an increase in asthma severity suggests a dose-response relationship (Nielsen et al., 2002). The National Co-operative Inner City Asthma Study clearly implied such a dose-response relationship between indoor allergen levels and asthma severity when it concluded that children allergic to cockroach allergens and exposed to high levels had a greater severity of asthma (Custovic et al., 2002).

Multiple studies have found that exposures to mold, including *Alternaria*, *Aspergillus fumigatus*, and *Cladosporium*, are also risk factors for the development of asthma (Halonen et al., 1997; Nielsen et al., 2002; Lin and Williams, 2003). In a study conducted in Tucson, Arizona, Halonen et al. (1997) found that children who had an immediate skin test response to *Alternaria* were more prone to develop asthma. Bush and Prochnau (2004) noted that in the United States, up to 80% of individuals with confirmed asthma have demonstrated positive reactivity to one or more species of mold. Although there is evidence of associations between asthma development and exposure to all mold (Table 2-10), the literature focuses primarily on the development of asthma in response to *Alternaria* exposure.

Exposure to *Alternaria*, and subsequently sensitization, has been increasingly recognized as a risk factor for the development and persistence of asthma, increased asthma severity, and potentially fatal asthma exacerbations (Nielsen et al., 2002; Bush and Prochnau, 2004). Similarly, a study conducted in Chicago by Targonski et al. (1995) found that mean mold spores, rather than tree, grass, or ragweed pollen, was associated with asthma-related deaths. Targonski et al. (1995) also found the risk of asthma-related deaths increased 2.16 times when the total *Alternaria* spore count was about 1,000 spores/m³. Overall, individuals sensitized to *Alternaria* appear to be more at risk for developing severe asthma compared to individuals with sensitivities to other aeroallergens (Bush and Prochnau, 2004).

Although there is evidence to support causal relationships between asthma development and exposure to both indoor allergens and mold, it is still unclear which class of aeroallergens is

the greater risk factor for asthma development. Some data, such as those provided by Halonen et al. and Targonski et al., suggest that mold may have a larger impact on asthma development. However, a study conducted on children in Virginia and New Mexico found that hypersensitivity to indoor allergens (e.g., cat and house dust mites) has a stronger association with asthma than hypersensitivity to mold (Lin and Williams, 2003).

Although these studies suggest that exposure to either indoor allergens or mold can cause asthma, other researchers have found the evidence for such associations inconclusive (Tortolero et al., 2002). As a result, some members of the scientific community feel they cannot definitively state that a direct relationship exists between indoor allergen or mold exposure, and asthma development. Overall, however, most of the literature suggests that exposure to indoor allergens and mold in sensitized individuals can result in a strong disposition to both the development of asthma and subsequent asthma exacerbations.

2.2.3. Atopic Dermatitis

Exposure to aeroallergens has also been implicated in the development of atopic dermatitis (eczema), and its development has commonly been found to predate the development of the more prevalent allergic diseases, allergic rhinitis and asthma (O'Connell, 2004). It has been estimated that atopic dermatitis affects 15 to 20% of the population of children worldwide (O'Connell, 2004).⁵ Studies examining the association between aeroallergen exposure and the development of atopic dermatitis have focused on individual responses to allergens by way of skin patch or skin prick tests. Most studies have found that 30 to 40% of patients with atopic dermatitis have positive skin patch tests to allergens (Whitmore et al., 1996). Clark and Adinoff (1989) found that the most common responses in skin patch tests on individuals with atopic dermatitis were for animal danders (53%), mites or dust (37%), mold (32%), and tree, grass, and weed pollen (14 to 35%). Adinoff et al. (1988) also observed positive skin prick tests for aeroallergens: 30% positive for pollen, 20% for mold, and 75% for dust, mites, and animals.⁶

Although these studies hint at an association between exposure to aeroallergens and the development of atopic dermatitis, there is conflicting evidence. Studying patients presenting with contact dermatitis, Whitmore et al. (1996) found that regardless of whether or not they were atopic, those suspected of having allergic contact dermatitis had a low incidence of presently

⁵O'Connell (2004) was the only study that provided a prevalence rate for atopic dermatitis. Unfortunately, the rate provided is worldwide, although the rest of the paper focuses on United States allergic illness rates.

⁶This study was not an epidemiological study. It was conducted to examine the possibility that atopic dermatitis may be triggered by aeroallergens in some individuals; therefore, the findings cannot be used to infer a causal association.

relevant allergic dermatitis when exposed to aeroallergens (Whitmore et al., 1996). Powell and Smith (1978), studying individuals sensitized to Russian thistle, observed dermatitis only in individuals who came into direct contact with the plant, rather than by way of exposure to its pollen.

Because of this contradictory evidence, the role of aeroallergens in the development of atopic dermatitis remains controversial (Whitmore et al., 1996). Whitmore et al. (1996) explain that the uncertainty surrounding the association is due partly to the fact that most of the studies do not include nonatopic control subjects. As a result, it is unclear if aeroallergens are the primary culprit in atopic dermatitis (Whitmore et al., 1996).

2.2.4. Cross-Reactivity

There is substantial evidence suggesting a causal relationship between aeroallergens and allergic diseases, but it remains unclear which aeroallergens are more highly associated with causing sensitization and subsequent disease development. The inability to develop a hierarchy of specific aeroallergens and their role in initiating an allergic response is primarily due to the cross-reactivity of aeroallergens—the ability of two or more aeroallergens, due to biochemical similarities, to elicit an allergic response in an individual who may be sensitized to only one of them. Multiple studies have found cross-reactivity among the aeroallergens implicated in causing allergic diseases (Table 2-11). Some aeroallergens not identified as being clinically relevant have shown cross-reactivity with those that are, which further complicates the ability to identify allergens associated with causing allergic diseases. For example, short ragweed is identified as a major cause of allergic rhinitis, but false and western ragweed all cross-react with short ragweed, which could result in an allergic response in a sensitized individual exposed to any of the ragweeds (White and Bernstein, 2003). Cross-reactivity is not specific to pollen; it has also been observed in mold and among asthma-related indoor allergens as well (Andersson et al., 2003; Halonen et al., 1997).

Table 2-11. Cross-reactivity of major clinically relevant aeroallergens

Latin name	Common name	Cross reactive aeroallergen(s)	Reference
Tree pollen			
<i>Acer negundo</i>	Box-elder	Red maple	Phipatanakul, 2005
<i>Acer rubra</i>	Red maple	Box-elder	Phipatanakul, 2005
<i>Alnus rubra</i>	Alder	Paper birch, white oak, red oak	White and Bernstein, 2003
<i>Betula papyrifera</i>	Paper birch	Alder, white oak, red oak	White and Bernstein, 2003
<i>Carya illinoensis</i>	Pecan	Black walnut	White and Bernstein, 2003
<i>Fraxinus americana</i>	White ash	Olive	White and Bernstein, 2003
<i>Juglans nigra</i>	Black walnut	Pecan	White and Bernstein, 2003
<i>Olea europaea</i>	Olive	White ash	White and Bernstein, 2003
<i>Quercus alba</i>	White oak	Paper birch, alder, red oak	White and Bernstein, 2003
<i>Quercus rubra</i>	Red oak	Paper birch, alder, white oak	White and Bernstein, 2003
<i>Ulmus americana</i>	American elm	Chinese elm, Siberian elm	Phipatanakul, 2005
<i>Ulmus parvifolia</i>	Chinese elm	American elm, Siberian elm	Phipatanakul, 2005
<i>Ulmus pumila</i>	Siberian elm	American elm, Chinese elm	Phipatanakul, 2005
Grass pollen			
<i>Cynodon dactylon</i>	Bermuda	Johnson	White and Bernstein, 2003
<i>Festuca elatior</i>	Meadow fescue	Bahia	White and Bernstein, 2003
<i>Holcus halepensis</i>	Johnson	Bermuda	White and Bernstein, 2003
<i>Lolium perenne</i>	Rye	Bahia	White and Bernstein, 2003
<i>Paspalum notatum</i>	Bahia	Timothy, meadow fescue, rye	White and Bernstein, 2003
<i>Phleum pratense</i>	Timothy	Bahia	White and Bernstein, 2003
Weed pollen			
<i>Amaranthus retroflexus</i>	Red root pigweed	Russian thistle	Phadia, 2002
<i>Ambrosia artemisiifolia</i>	Short ragweed	Mugwort	White and Bernstein, 2003
<i>Artemisia vulgaris</i>	Mugwort	Ragweed	White and Bernstein, 2003
<i>Salsola kali</i>	Russian thistle	Red root pigweed	Phadia, 2002
Mold			
<i>Alternaria alternata</i>	N/A	<i>Epicoccum nigrum</i>	Levetin, 2006
<i>Epicoccum nigrum</i>	N/A	<i>Alternaria alternata</i>	Levetin, 2006
Indoor allergens			
<i>Dermatophagoides farinae</i> ; <i>Dermatophagoides pteronyssinus</i>	Arthropods (domestic mites)	Cross reactive with one another	Phipatanakul, 2005

Note: This table includes only those aeroallergens that have been implicated as being cross-reactive with another aeroallergen.

3. HISTORICAL TRENDS IN AEROALLERGENS AND ALLERGIC DISEASES IN THE UNITED STATES

The amount and distribution of aeroallergens, as well as the prevalence of allergic diseases in the United States, is likely to change over time. This section examines past trends and current levels of both aeroallergens and allergic diseases.⁷

3.1. AEROALLERGENS

During approximately the last 30 years, numerous studies have examined historical trends in aeroallergen production and distribution, most notably for pollen and some types of mold. Most studies observing pollen levels over time have found year-to-year fluctuations but no major trends. Observing pollen trends in Philadelphia and Southern New Jersey, Dvorin et al. (2001) found that although all pollen levels fluctuate yearly, tree pollen demonstrates a larger fluctuation than either grass or weed pollen. In a 21-year study of airborne pollen levels in Switzerland, Clot (2003) observed no major change in the yearly pollen abundance for the majority of pollen species studied.⁸

In some studies, the overall abundance of pollen in an area did change dramatically over time, but this was due to specific nonclimatic factors. For example, Emberlin et al. (1999) reports a study observing pollen trends conducted at three sites within the UK—London, Cardiff, and Derby—which found pollen levels decreased in Derby and London while they significantly increased in Cardiff. The substantial changes in pollen levels at each site were attributed to changes in land use that occurred during the study period (Burr, 1999). Similarly, Sneller et al. (1993) found a dramatic increase in pollen levels over 5 decades in Tucson, Arizona as a result of the importation of certain tree species to the city due to changing architectural and landscape preferences. With the exception of cases of anthropogenic changes, which altered the abundance of aeroallergen levels observed in Emberlin (1994) and Sneller et al. (1993), however, pollen levels have tended to remain fairly consistent on a year-to-year basis.

⁷This section of the report does not address other factors that have been implicated in affecting the overall trends of aeroallergens, specifically climate change.

⁸Clot (2003) found that *Alnus*, *Taxus/Cupressaceae*, and *Artemisia* pollen were significantly higher at the end of the 20-year study than at the beginning, but it is unclear why the pollen levels for these four species increased over time.

Studies have shown that the duration of the pollen season has remained fairly stable over time. In their 6-year study of pollen levels in Philadelphia and Southern New Jersey, Dvorin et al. (2001) observed that the pollen season did not change significantly. They found late April to early May and early September consistently represented the significant spring and fall periods, respectively, of airborne pollen prevalence (Dvorin et al., 2001). These findings agree with those of Kosisky and Carpenter (1997), who found in a study observing tree pollen over a 5-year period in Washington, D.C. that April remained the month with the highest weekly average concentrations over the study period (Kosisky and Carpenter, 1997). We conclude that the time frame for these studies (5 and 6 years, respectively) may not be long enough to examine trends in pollen season.

Although these studies suggest that the duration of the pollen season has been relatively stable, other studies suggest a trend towards an earlier initiation of the pollen season. Emberlin et al. (2002) and Clot (2003) both observed a shift in the timing of the pollen season during long-term pollen observation studies. Clot (2003) observed strong trends towards an earlier pollen season for tree pollen and a less remarkable shift for grass and weed pollen. Emberlin et al. (2002) observed a trend towards an earlier start date for the *Betula* (Birch) pollen season by about 6 days, but ranging up to 30 days. Preliminary data suggest that a change in the initiation of the pollen season may not influence its overall duration (Clot, 2003).⁹ It should be noted that warming has occurred mainly over the past 30 years and that interannual variations make it hard to detect trends over time. We would need a 2–3 decade record of pollen counts measured in a consistent way to have a chance of observing a trend.

While pollen levels have remained fairly consistent over time, this is not the case for mold. The evidence suggests a possible increase in the concentration of some types of mold. *Epicoccum nigrum* has recently been sprayed onto sunflowers to control sunflower head rot (Burge, 2002). A continued increase in the use of *Epicoccum nigrum* and other types of mold as biocontrol agents might increase the proportion of outdoor mold that is associated with allergic diseases in the environment (Burge, 2002). Although the increased use of mold commercially could result in an increase in mold in the environment, an increase in the abundance of *Alternaria* has already been observed. In a study conducted in Derby, UK from 1991–1998,

⁹Emberlin et al. (2002) did not study the duration of the pollen season.

Corden and Millington (2001) found a dramatic increase in the number of days with *Alternaria* spore counts above 50 spores/m³.

3.2. HISTORICAL TRENDS OF ALLERGIC DISEASES

If aeroallergen levels remain fairly stable, the prevalence of allergic illness would be expected to remain stable as well. The evidence suggests, however, that this is not the case. The prevalence of allergic diseases in the United States has increased over the last 30 years (Figure 3-1 and Figure 3-3). This upward trend in the United States appears to be mirrored in other countries, too. In the Copenhagen Allergy Study, Linneberg et al. (2000) found the prevalence of specific IgE antibodies to at least one allergen in the cohort increased significantly from 1990 to 1998, which coincided with an increase in the prevalence of allergic rhinitis. Linneberg et al. (2000) also cite Nakagomi et al. (1994), who found an increase in IgE positivity from 21.4% in 1978 to 39.4% in 1991 to one or more of 16 allergens in schoolgirls in Japan. These findings and data collected via surveys by the CDC suggest the prevalence of allergic diseases has increased over time, but that finding is suspect, given the lack of sufficiently long records using consistent measurement methodologies. We conclude that allergic illness trends described here are consistent with the overall body of scientific literature but not of adequate duration to support certain trends.

The perceived increase in allergic diseases over time has not been adequately explained. It might be expected that an increase in the prevalence of allergic diseases would imply a corresponding increase in the levels of their associated aeroallergens, but, as noted above, we do not yet have sufficient data and research to determine whether this has occurred. Therefore, it is possible that there are other factors to explain the increase in the prevalence of allergic diseases. The rate at which the prevalence of respiratory allergies has been increasing argues against the trend being solely attributed to genetic factors. One theory, known as the “hygiene hypothesis,” suggests that larger family size, exposure to respiratory infections, microbial exposure, and exposure to other bacterial components such as endotoxin have a protective effect against the development of hay fever and other allergic diseases (Phipatanakul, 2005). The smaller family sizes now observed in Western countries have reduced children’s exposure to cross infections, which may prevent the development of hay fever (Von Hertzen, 1998). Evidence supporting this hypothesis comes from studies that have found a negative correlation between the prevalence of

allergic rhinitis and the number of older siblings, implying that increased family size reduces a child's risk of developing allergic rhinitis (Phipatanakul, 2005). A similar protective effect has also been observed for children who have early exposure to day care after 1 year of age (Phipatanakul, 2005). Unfortunately, recent studies have been unable to identify single or multiple determinants in lifestyle or home environment that could significantly affect disease development (Linneberg et al., 2000).

3.2.1. Asthma

Over the last 30 years, there has been a significant increase in the prevalence of asthma (Figure 3-1). It is not yet clear what is driving the observed increase in asthma prevalence, because many factors may influence its development. As noted above, aeroallergens have a significant impact on asthma development. It is unclear what percentage of asthma cases each year can be attributed to exposure to aeroallergens, and aeroallergens have also not shown a corresponding increase that could potentially account for some of the increase in asthma prevalence (Nielsen et al., 2002).

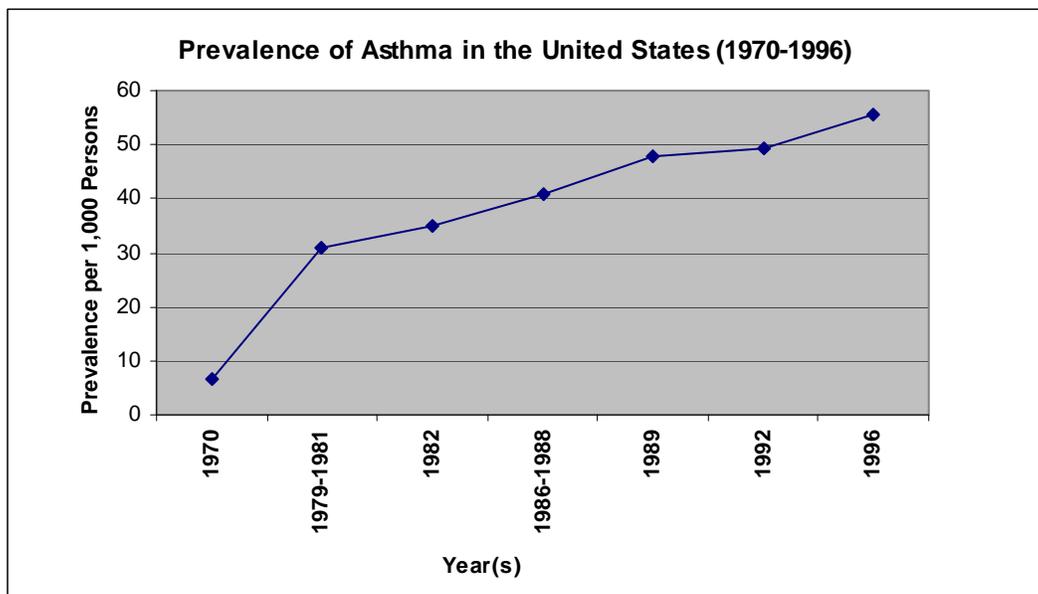


Figure 3-1. Prevalence of asthma in the United States from 1970 through 1996.

Sources: National Center for Health Statistics (NCHS, 1973, 1985, 1989, 1992, 1993, 1994, 1999).

The increase in the prevalence of asthma has been particularly acute among individuals of low socioeconomic status (Phipatanakul, 2005; Hamilton and Eggleston, 1997). This has been believed to be primarily the result of higher levels of exposure to indoor allergens, especially cockroaches, in this population (Phipatanakul, 2005; Hamilton and Eggleston, 1997). This trend may extend beyond the inner city; recently, cockroach allergen has been found to be more common in suburban middle class homes with asthmatic children than previously thought (Hamilton and Eggleston, 1997; Hamilton, 2005).

Figure 3-2 shows that asthma prevalence has increased in all regions of the United States, with the most significant increase occurring in the Northeast. Some recent studies have shown a possible stabilizing of asthma prevalence, but it is unclear if this is a true effect or a result of multiple definitions being used to identify asthma. These studies have not shown consistent results across geographic regions or demographic characteristics, but instead have shown a heterogeneity of patterns of asthma diagnosis, symptoms. Allergic sensitization of the assessment of the trends observed in asthma prevalence is thus difficult because of the heterogeneity of the disease and the fact that there is no recognized standard used to make a diagnosis (Lawson and Senthilselvan, 2005).

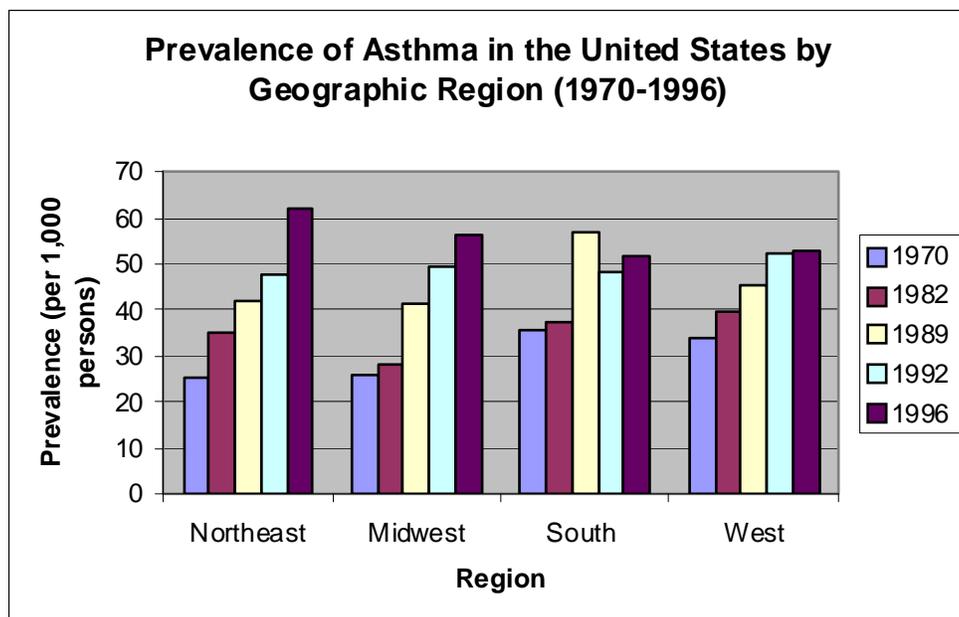


Figure 3-2. Prevalence of asthma in the United States by geographic region from 1970 through 1996.

Sources: NCHS (1973, 1982, 1985, 1989, 1990, 1992, 1994, 1999).

3.2.2. Allergic Rhinitis

Consistent with the findings for asthma, there has also been an increase in the prevalence of allergic rhinitis (hay fever) in industrialized countries over the last 30 years (Figure 3-3). Similarly, because this increase is not accompanied by a corresponding increase in pollen abundance, its origins remain unclear (Clot, 2003).

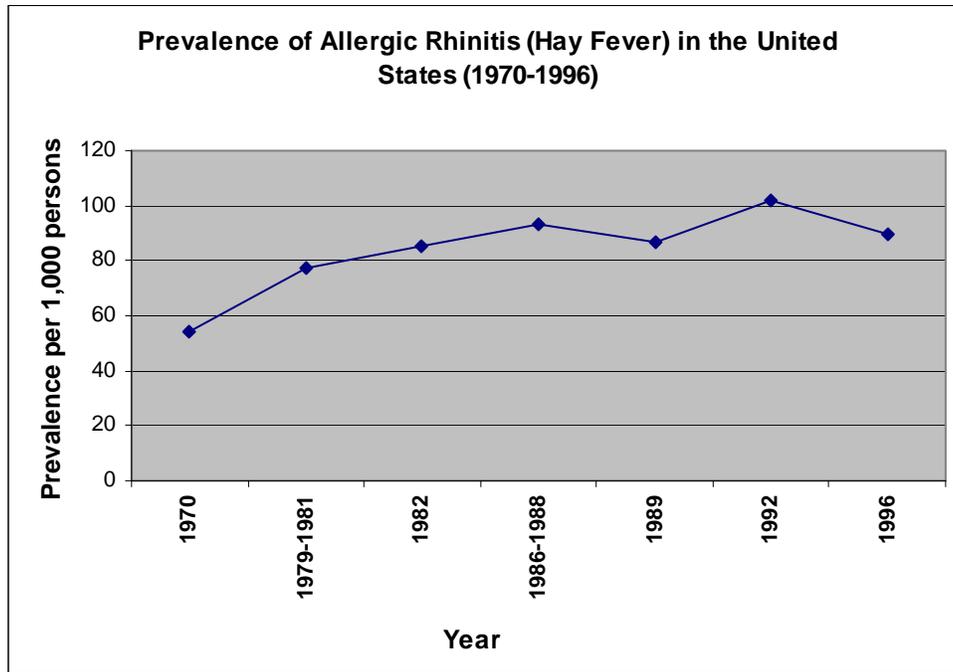


Figure 3-3. Prevalence of allergic rhinitis (hay fever) in the United States from 1970 through 1996.

Sources: NCHS (1973, 1982, 1985, 1989, 1990, 1992, 1994, 1999).

Numerous studies have shown that, unlike asthma, allergic rhinitis has a higher prevalence in individuals of higher socioeconomic status (Phipatanakul, 2005). It is unclear why this might be the case, but according to the hygiene hypothesis, a decrease in exposure to certain infections may account for this observation.

As shown in Figure 3-4, there have been significant increases in the prevalence of allergic rhinitis in all regions of the United States, with the greatest number of cases consistently occurring in the West. The sampling protocols used to obtain prevalence rates, however, may not accurately reflect the true prevalence. Studies have observed the prevalence through two

avenues: questionnaires/interviews and physician diagnosis, both of which tend to underestimate the actual prevalence of the disease (Phipatanakul, 2005).

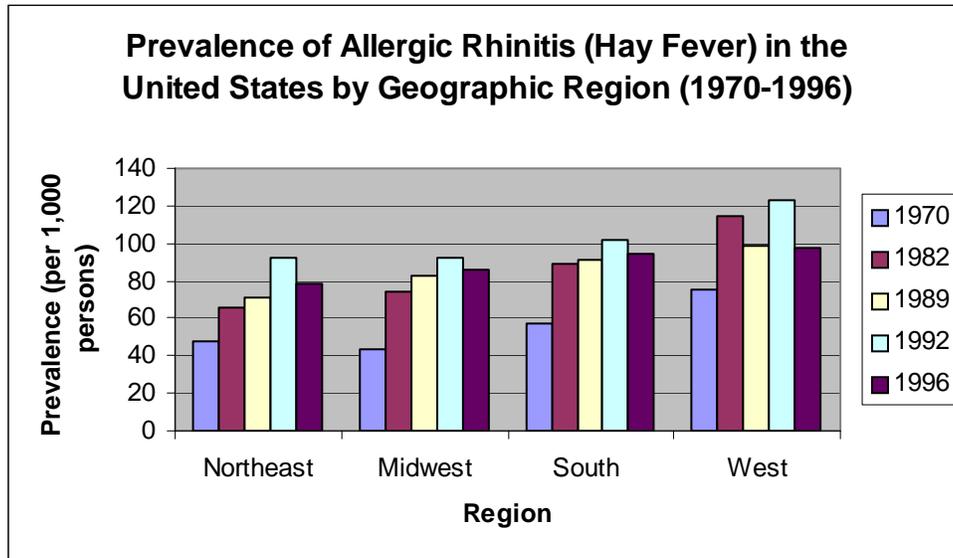


Figure 3-4. Prevalence of allergic rhinitis (hay fever) in the United States by geographic region from 1970 through 1996.

Sources: NCHS (1973, 1982, 1985, 1989, 1990, 1992, 1994, 1999).

3.2.3. Atopic Dermatitis

There is only limited information on the historical trends of atopic dermatitis. Approximately 15 to 20% of the worldwide childhood population is currently afflicted with the illness, but considerable evidence suggests the prevalence of atopic dermatitis may be increasing above the 15 to 20% now observed (O’Connell, 2004). Because of the controversy surrounding the diagnosis of atopic dermatitis, as discussed by Whitmore et al. (1996), it will be possible to accurately reflect the prevalence of atopic dermatitis over time only when studies are conducted with adequate controls.

4. IMPACTS OF CLIMATE CHANGE ON AEROALLERGENS

Climate change, caused in part by increased atmospheric CO₂ and other greenhouse gas concentrations, may result in increases in temperature, precipitation, humidity, and extreme weather events. These factors, including CO₂ concentration, can impact the production, distribution, dispersion, and allergen content of aeroallergens and the growth and distribution of organisms that produce them (i.e., weeds, grasses, trees, and fungus). Shifts in aeroallergen production and, subsequently, human exposures may result in changes in the prevalence and severity of symptoms in individuals with allergic diseases. This section reviews the potential and observed impacts of climate change on aeroallergen production, distribution, dispersion, and allergen content, and discusses how climate-related changes in aeroallergen production may lead to indirect impacts on allergic diseases.

4.1. PRODUCTION OF AEROALLERGENS

It has generally been observed that the presence of elevated CO₂ concentrations and higher temperatures stimulate plants to increase photosynthesis, biomass, water use efficiency, and reproductive effort (The Center for Health and the Global Environment, 2005; Jablonski et al., 2002). However, these relationships are complex and likely differ among taxa and species. Short-term responses to climate change (i.e., over 10 to 20 years) might involve changes in plant phenology and biochemistry. This is consistent with a recent meta-analysis that indicates the current rate of phenologic advance is 5 days per decade for numerous species of plants (Root et al., 2003). A key finding of the National Assessment Synthesis Team (NAST; Melillo et al., 2001) was that over the next few decades, climate change is very likely to lead to increased plant productivity and carbon storage for many parts of the country, especially those areas that become warmer and wetter (Melillo et al., 2001; Joyce et al., 2001). We might infer, then, that pollen production in these areas, on average, would be expected to increase. The NAST also found that areas where soils dry out during the growing season, such as the Southeast under certain scenarios, are likely to see reduced productivity and carbon storage, and hence, less pollen production. The following subsections review specific studies on how climate change may alter plant and fungal reproductive responses in the United States.

4.1.1. Pollen

4.1.1.1. *Tree Pollen*

Research on the potential effects of climate change on tree pollen production in the United States is limited. Researchers have tried to identify important climatic variables for seasonal forecasting of tree pollen seasons, but often these models do not account for climate change and are specific to species and geographic locales outside of the United States. However, to the extent that this research successfully identifies strong projections of pollen season severity, one can infer that changes in those projectors may directly impact pollen production. Overall, research shows pre-season temperature and precipitation to be the most consistent projectors of tree pollen seasons. The relevant details of studies on tree pollen production are presented below using the framework of start date and pollen season severity.

Levetin (2001) reported that cumulative season total pollen for *Juniperus* (cedar), *Quercus* (oak), *Carya* (hickory and pecan), and *Betula* (birch) increased significantly during a 14-year period beginning in 1987 in Oklahoma. Meteorological data also showed a significant increase in average winter temperatures. Correlations between winter temperatures and pollen counts were not significant. The author noted that the cause of the increasing pollen count trend was unknown and could include climate change, urbanization, or evolving landscaping patterns. Lo and Levetin (2007) found increased cumulative season total pollen counts for *Cupressaceae* pollen increased from 1986–2007 in Tulsa, OK, although there was no significant change in *Ulmus* pollen counts, nor was the observed seasonal start date significant. Pollen counts for both taxa were significantly positively correlated with daily minimum, mean, and maximum temperatures and significantly negatively correlated with precipitation.

United States researchers examined pollen counts in New England before and after the occurrence of an El Niño event that started in mid-1997 and continued until the summer of 1998 (Freye and Litwin, 2001). While El Niño is a cyclical climatic event that is not necessarily associated with climate change, it can serve as an example of the impact of short-term variability on pollen production. This El Niño was similar to projected climate change in that precipitation was 2 to 8 inches greater than normal during the winter and spring of 1998, and temperature was 4 to 6°F higher than normal during winter of 1998. The authors observed that, relative to 1997 and 1999, maximum pollen counts were higher and occurred about 2 to 4 weeks earlier for most tree types during 1998, but a statistical analysis of the difference is not provided. Similarly,

Reiss and Kostic (1976) found strong correlations (r^2 range 0.85 to 0.94) between pollen season severity and spring and summer minimum temperatures and mid-spring precipitation amounts in New Jersey, but they did not specify pollen types. Oak pollen counts in the San Francisco Bay Area were strongly correlated with total rainfall during the previous year (Weber, 2003a, b).

In Cordoba, Spain, researchers studied the influence of meteorological parameters on *O. europaea* L pollen and found that cumulative variables for temperature and sunlight hours were the most common significant (Students $t < 0.05$) projectors of pollen concentration in regression analysis (Vazquez et al., 2003). In Poland, researchers found positive significant ($p < 0.05$) correlations between air temperature and birch pollen concentration but negative nonsignificant correlations with poplar pollen, indicating the need for species-specific analysis (Puc and Wolski, 2002). A study of birch pollen in two sites in Denmark found that the pollen season started earlier, peaked earlier, and ended earlier, and had increased seasonal total pollen counts, higher peak count levels, and more days with pollen counts greater than zero. The study attributed the earlier start of the pollen season to higher winter and spring temperatures (Rasmussen, 2002).

International research to identify trends in pollen season start dates, using databases, including species relevant to the United States, such as birch (*Betula*) and olive (*Olea europaea* L.), is also informative. Even in this case, however, there is limited assessment of changes in pollen production. Long-term pollen monitoring data are available for several locations in Europe, and researchers have analyzed these data for changes in pollen season start dates. Overall, while several analyses show earlier start dates, there is an indication that the observed effect may be specific to species and geography. Clot (2003) analyzed time series of 21 years of data in Switzerland. Using the Seasonal Pollen Index (SPI), Clot (2003) found that there was no major change in the abundance of pollen among most of the 25 taxa studied. There were a few exceptions to this. Linear trend analysis showed increases ($p < 0.05$) of pollen quantities were observed for *Alnus* (alder), *Ambrosia* (ragweed), *Artemisia* (mugwort), and *Taxus/Cupressacea* (yew/cypress), and decreases were seen in *Ulmus* (elm). Clot (2003) also observed that the duration of the pollen season did not appear to change but that 71% of the start or end dates of the pollen season occurred significantly earlier in the year. The average observed advance was 0.84 days/year, and a stronger reaction was found in trees to climate change than in weeds and grasses (Clot, 2003).

Frenguelli (2002) reviewed 20 years of data, from 1982 to 2001, on airborne pollen and mean air temperature in Perugia (central Italy) and reported an increase in annual mean temperature of 0.7°C, with the months of February, May, June, and August experiencing the greatest increases. Results show the pollen seasons of most taxa starting earlier, and for several taxa, the season duration is shorter as well. An exception is *Urticaceae* (nettle), which experienced an increased seasonal duration.

Emberlin et al. (2002) investigated relationships between changes in start dates of birch pollen seasons and changes in spring temperatures, using daily birch pollen counts from six metropolitan cities in Europe from 1982–1999. London, Brussels, Zurich, and Vienna showed trends towards earlier start dates, and a regression analysis indicated the mean start dates at these sites would advance by about 6 days over the next 10 years (Emberlin et al., 2002). In Kevo, Finland the opposite effect was observed, with cooler springs and therefore later starts of 6 days on average per decade. While the data are suggestive of changes in the timing of pollen season starts, there was no assessment of whether or not this would lead to greater pollen production or allergen content.

In Andalusia, Spain, Galan et al. (2005) compared the start of *O. europaea* L. pollen season and heat accumulation over a selected temperature threshold while investigating the influence of topography on the results. The authors used pollen and meteorological data from 1982–2001 for five sites in central and eastern Andalusia. The study found that all of the study sites had increasingly earlier start dates during the study period. The authors used the Hadley Climate Model (a regional model developed by the Hadley Meteorological Centre, UK) to estimate the impact of projected climate change on the olive tree's flowering phenology. Their results indicated an advance of 1–3 weeks by the end of the century. García-Mozo et al. (2006) found that *Quercus* species trees showed earlier start dates in fourteen different locations throughout Spain from 1992–2004, most likely due to the increased temperatures seen at those sites over the same time period. Using projected meteorological changes from Regional Climate Models and an externally validated growing degree days forecasting model, they projected that the *Quercus* pollen season could start on average one month earlier in Spain and pollen counts could increase by up to 50%, with the largest increases in inland Mediterranean locations. As with previous research, however, it is not clear how a shift in pollen season start may affect production. Researchers have also found advances in start dates in Japanese cedar (*Cryptomeria*

japonica), as well as an increased pollen count and an extended pollen season (Teranishi et al., 2000).

Glassheim et al. (1995) examined the short-term (i.e., 1-day lag) relationship between observed tree pollen counts from elm, juniper, maple, cottonwood, and pine in Denver, Colorado and a selection of independent meteorological variables. With the exception of pine, none of the tree pollen studied for the 5-year period appeared affected by temperature. However, this short-term type of analysis may have limited relevance to seasonal pollen production and climate change. The authors did observe modest negative correlations with both precipitation and relative humidity, which is likely due to “scrubbing” or particle adsorption (to raindrops), which removes pollen from the air.

In summary, pre-season temperature and precipitation are important projectors of tree pollen production. To the extent that climate change results in changes in these two meteorological variables, then, we would expect corresponding changes in tree pollen production, all else equal, although the evidence to date suggests that the nature of the changes may be region and species-specific. One United States study observed a trend of increasing pollen production in Oklahoma (Levetin, 2001). Changes in phenology (start date) appear to be a relatively consistent finding, especially for European species. However, in most studies, the change in start date did not correspond to a lengthening of the pollen season. Additionally, it is unclear whether the phenologic changes have an effect on total pollen production or allergen content. The literature does not provide clear evidence of changes in phenology in United States species; however, this may be due to limitations in data.

4.1.1.2. *Grass Pollen*

As with tree pollen, research on the potential effects of climate change on grass pollen production in the United States is limited in scope at present. Overall, forecast models show temperature and precipitation to be the most consistent projectors of grass pollen seasons, but these models do not directly take into account climate change and are again specific to geographic locales, most of which are not in the United States.

As described above, United States researchers Freye et al. (2001) examined pollen counts in New England before, during, and after the occurrence of an El-Niño event. With the

exception of an earlier peak in 1998, overall grass pollen concentrations did not appear to be affected. The details of selected research are reviewed below.

Contrary to general projections of increased production, one of the longest data series for grass pollen suggests earlier starts but declining annual counts and severity in England. These changes are most likely due to land use trends, such as declining agriculture and pasture areas (Emberlin, 1994). In England, Emberlin et al. (1999) used data from 1961–1993 at Cardiff, Derby, and London to project total seasonal catches, the severity of seasons in terms of the number of days with high counts, and the start dates of seasons. The authors found that at two of the sites (Derby and London) the annual counts and severity declined but at different rates, while at the third site (Cardiff), annual counts and severity increased in the 1960s, declined in the 1970s, and rose again in the 1980s. There was a trend towards earlier start dates at the Derby site, a less pronounced trend at Cardiff, and a trend towards later starts in London. In models, the most important climatic variables influencing the broad features of grass pollen seasons (e.g., seasonal cumulative pollen counts and peaks) were cumulative rain and temperature, but the importance of these variables differed by site and was overshadowed by the influence of land use. The authors conclude that the contrasting patterns both in pollen records and land use changes among the three sites underscore the need for regional data. In a prior analysis, they reached similar conclusions, suggesting that changes in pollen production will vary by region such that many central areas north of the Alps could have longer grass pollen seasons, while grass pollen concentrations are likely to decrease in the southern Mediterranean area during summer months (Emberlin, 1994). The regional differences reflect the interaction of climate change at different latitudes and topography, i.e., reduced snow cover in the Alps and increasing drought in the Mediterranean; both of which must be evaluated against land use trends as well. In contrast, Clot (2003) reviewed 21 years of grass pollen data from a single trap in Switzerland and found an earlier start date (–14 days) but no significant change in the duration or intensity of the pollen season.

Puc and Puc (2004) analyzed grass pollen seasons in western Poland from 2000 to 2003 to evaluate relationships between meteorological parameters and *Poaceae* (grass) pollen counts. The authors found that air temperature and relative humidity were most consistently correlated with pollen counts.

In Australia, grass pollen accounts for 71% of the total atmospheric pollen counts (Green et al., 2004). Green et al. (2004) evaluated grass pollen counts and associations with meteorological parameters in Brisbane, Australia from 1994 to 1999. The authors found that daily grass pollen counts were positively associated ($p < 0.0001$) with maximum and minimum temperature each sampling year. Precipitation was observed to “scrub” or remove pollen grains from the atmosphere during significant periods of rainfall.

Glassheim et al. (1995) examined the short-term (i.e., 1-day lag) relationship between meteorological variables and grass pollen in Denver, Colorado. The authors found that grass pollen counts during the period 1987–1991 were correlated with high temperature ($r = 0.305$, $p < 0.001$) and less so with percent daily sunshine ($r = 0.149$, $p < 0.006$) and were negatively associated with precipitation ($r = -0.227$, $p < 0.001$) and relative humidity ($r = -0.430$, $p < 0.006$). Glassheim et al. (1995) also found that correlations were not consistent from year to year, suggesting the intraseasonal meteorological conditions that determine pollen counts may vary from year to year or that pre-season conditions are more important.

Research in Spain also indicates that pre-season meteorological variables are more important and consistent determinants of seasonal pollen load than are day-to-day weather conditions (Gonzalez Minero et al., 1998). Declines in grass pollen were observed for the period 1987–1996. This was attributed to several years of drought, a potentially important but less projectable feature of climate change. Pre-seasonal rainfall, temperature, and average monthly humidity in Spain were strong projectors of total grass pollen count (Burr, 1999; Gonzalez Minero et al., 1998).

In summary, temperature and precipitation are important factors in grass pollen production, but more so in terms of pre-season conditions than day-to-day meteorological conditions during the pollen season. The correlation with precipitation is not straightforward as pre-season precipitation may increase pollen counts but in-season precipitation tends to “scrub” or remove pollen from the air. To the extent that climate change results in changes in these two meteorological variables, we would expect some changes in grass pollen production. In Europe, earlier start dates have been observed, as well as declines in production, but this is attributed to changes in land use. The literature does not provide clear evidence of changes in start dates or production in United States species.

4.1.1.3. *Weed Pollen*

Common ragweed (*Ambrosia artemisiifolia* L.) is recognized as a significant cause of allergic rhinitis in the United States, and there is relatively more research on the response of this weed to climatic variables, especially in the context of climate change. Specifically, several researchers have used controlled environments to examine ragweed response to carbon dioxide levels and temperature, the two covariates for which models reliably project increased levels in the future. The following section details the studies that observed the association between climatic variables and ragweed production.

Ziska and Caulfield (2000) tested whether the increase in atmospheric CO₂ concentrations since the Industrial Revolution and projected future increases may alter growth and pollen production of common ragweed. Experiments were conducted using a controlled environmental chamber to measure the growth and pollen production of common ragweed from preindustrial levels of CO₂ (280 μmol/mol) to current concentrations (370 μmol/mol) to a projected 21st century concentration of 600 μmol/mol. The experiments showed that pollen production increased approximately 132% from preindustrial levels to current levels of carbon dioxide and approximately 90% for current to projected future levels of carbon dioxide. The observed increase of pollen production from the preindustrial CO₂ concentration was due to an increase in the pollen per floral spike (at 370 μmol/mol) and number of floral spikes (at 600 μmol/mol).

Wayne et al. (2002) found similar results using environmentally controlled greenhouses to grow stands of ragweed plants from seed through flowering stages at CO₂ concentrations of 350 vs. 700 μL/L. The authors found that stand level pollen production was 61% higher in elevated versus ambient CO₂ environments ($F = 15.16, p = 0.005$). The authors comment that previous studies with ragweed have shown that adding essential resources to stands (e.g., nitrogen) results in plants investing in proportionally more male pollen-generating reproductive structures versus female pollen-accepting reproductive structures, consistent with the observations of Ziska and Caulfield (2000).

Ziska et al. (2003) followed up on the chamber studies conducted by Ziska and Caulfield (2000) and Wayne et al. (2002) with field studies. The authors used existing temperature/CO₂ concentration gradients between urban and rural areas in Maryland to examine the quantitative and qualitative aspects of ragweed growth and pollen production. In addition, pollen was

subjected to immunochemical analysis to quantify content of the allergen protein AMB A 1. Average daily (24-hour) values of CO₂ were 30 and 31% higher in 2000 and 2001, respectively, within an urban environment vs. at a rural site; air temperature was 1.8 and 2.0°C higher in 2000 and 2001, respectively, within the urban environment. Overall, the results demonstrated small but measurable phenologic differences as a function of both temperature and CO₂ concentration. Ragweed grew faster, flowered earlier, and produced significantly greater aboveground biomass and ragweed pollen at urban locations, which have a higher CO₂ concentration and temperature than at rural locations. However, a significantly ($p < 0.01$) higher quantity of antigenic protein was extracted from pollen at the rural site relative to other sites.

Ziska et al. (2007) documents the continued evaluation of the urban to rural transect in Maryland that they reported on previously in Ziska et al. (2003). The authors continued to monitor the three plot locations through 2005 and found that the rural and suburban plots continued to increase in ragweed biomass, but, after 2003, the urban plot declined significantly despite the continued higher temperature and CO₂ concentrations at the urban location. They document that with the increased biomass, which was observed in the urban plots associated with higher temperatures and CO₂, there is also higher litter accumulation, which can hinder the growth of new seedlings, and the suburban plot started to show biomass decline in 2005, which could signal a similar mechanism after high biomass. Another possible reason for the decline could be a decrease in soil disturbance, which ragweed requires for growth.

Rogers et al. (2006) designed a study to examine the potential impact of earlier arrival of spring and the interaction with CO₂ concentrations on ragweed pollen productivity. The authors used climate controlled greenhouses to test (1) whether variability in the onset of spring alters the rate and magnitude of ragweed development, flowering phenology, and seasonal pollen production; and (2) whether atmospheric CO₂ concentrations directly alter ragweed development and productivity, and influence plant responses to climatic variability. Cohorts of ragweed seeds were released from dormancy at three 15-day intervals and grown at ambient concentration or 700 ppm CO₂ concentration. Carbon dioxide treatment did not significantly affect days to anthesis or anthesis date. The authors found the timing of spring onset was the primary factor in a model fit for indicators of plant growth and, thus, pollen production. At ambient CO₂ concentration, the earlier cohort had 54.8% greater pollen production than the latest cohort. However, in the early cohort, pollen production was similar under ambient and high CO₂

concentrations, but in the middle and late cohorts, high CO₂ concentration increased pollen production by 32 and 55%, respectively compared to ambient CO₂ levels (see Figure 4-1). Thus, at elevated CO₂ concentrations, pollen productivity appears less sensitive to variability in season onset. The authors project that in future climates with elevated CO₂ concentrations, pollen production will be just as robust in years with late springs as those with early springs.

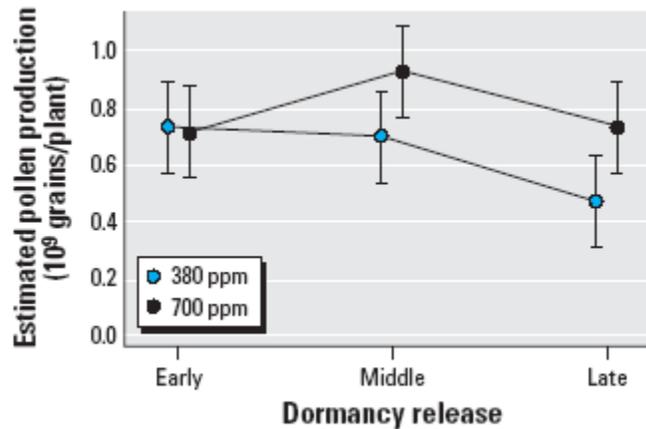


Figure 4-1. Pollen production in *A. artemisiifolia* for three springtime dormancy release cohorts grown at two CO₂ concentrations (380 ppm and 700 ppm).

Notes: Error bars indicate 95% confidence intervals.

Source: Rogers et al. (2006, Figure 4).

Wan et al. (2002) experimented with changes in temperature and clipping ragweed plants to determine if either or both of these factors made a difference in ragweed plant growth and pollen production. The warmed plots had 1.2°C air temperature, and the soil temperature was 1.8°C higher in the heated plots without clipping and 2.7°C in the heated plots with clipping, as clipping showed to increase the soil temperature possibly by exposing more of it to the heat source. The ragweed plants in the warmed plots showed many significant changes, including increases in the number of stems, total biomass, percent coverage, pollen diameter, and total pollen production. The authors hypothesized many possible reasons for these changes, including that ragweed is well adapted to disturbed warm areas and is taller than other plants; that warming

extends the growing season and therefore enhances survivorship; and that experimental warming may have increased nitrogen availability in the soil, which promotes the growth of ragweed. Whatever the reason, this experiment implied that warmer temperatures may increase the growth and pollen production of ragweed.

Glassheim et al. (1995) calculated correlation coefficients between observed pollen counts in Denver, Colorado and a selection of independent meteorological variables. The prevalent weeds analyzed were ragweed, sage, and the chenopod/amaranth group (pigweed). High and low temperature were most strongly correlated with total weed pollen counts during 1987–1991 ($r = 0.603$, $p < 0.001$). This is consistent with the work by Rogers et al. (2006), which indicates that an early start to the growing season, as indicated by minimum temperature, results in larger, more productive plants. Similar observations of increased biomass have been observed in CO₂ enrichment experiments with poison ivy (Mohan et al., 2006). While poison ivy does not produce aeroallergens per se, the smoke generated from burning poison ivy can be highly allergenic.¹⁰ Stefanic et al. (2005) found similar results in the Republic of Croatia, reporting that mean and minimum annual air temperatures were significantly correlated with the amount of ragweed pollen in the air during 2001–2003. Similar to Glassheim et al. (1995), however, the authors found inconsistency in relationships from year to year.

Overall, studies of ragweed in controlled environments and in field studies show that pollen production can be expected to increase with increased temperature and carbon dioxide levels. The experimental results have demonstrated that doubling carbon dioxide levels from current (350 $\mu\text{mol/mol}$) to projected future levels (i.e., 700 $\mu\text{mol/mol}$) would result in a 60 to 90% increase in ragweed pollen production (Ziska and Caulfield, 2000; Wayne et al., 2002). Field studies of differences between rural and urban growth patterns also clearly show that ragweed flowers earlier and produces greater amounts of pollen at urban locations compared to rural locations (Ziska et al., 2003). Rogers et al. (2006) confirmed this effect by showing that the timing of spring onset (i.e., early start) was the primary factor in a model fit for indicators of ragweed growth and, thus, pollen production. The higher allergen concentration in pollen at the rural site, however, highlights the need for caution in making inferences about public health implications.

¹⁰Personal communication with J. Patz, June 9, 2006.

4.1.2. Mold

Assessment of mold production in response to climate change is mainly derived from observational analyses of long-term data sets. Other assessments of mold production are essentially short-term forecasts of intraseasonal spore counts and are strongly dependent on whether the mold is a wet- or dry-weather type. Details of these studies are presented below.

Katial et al. (1997) analyzed 8 years of spore count data for *Cladosporium*, *Alternaria*, and *Epicoccum* in Denver, Colorado. The authors found a statistically significant year effect ($p < 0.01$), indicating a positive linear trend in *Cladosporium* spore counts over time. No trends were observed for *Alternaria* or *Epicoccum*. In addition, there were no trends in annual temperature, precipitation, or humidity to account for the trend in *Cladosporium* spore counts. The authors suggest urbanization of Denver as a potential explanation for the increase in *Cladosporium*, but the mechanism for the increase (e.g., soil disturbance, changing land use, etc.) is not clear. They found that for *Cladosporium*, average temperature ($p < 0.02$) and humidity ($p < 0.01$) were positively associated with spore counts, while precipitation was negatively associated with spore counts ($p < 0.01$). Neither *Alternaria* nor *Epicoccum* showed correlations with meteorological parameters.

Corden and Millington (2001) examined *Alternaria* concentrations during 1970–1998 in Derby, UK and found an upward trend, which increased markedly after 1992. Their analysis also showed an earlier start date and a longer season over time. A further analysis by Cordon et al. (2003) comparing *Alternaria* counts in Derby, UK and Cardiff, UK hypothesized that the earlier start date, longer season, and higher counts in Derby compared to Cardiff could be due to increased cereal production in fields near Derby and possibly to changes in climate as evidenced by low *Alternaria* counts during a drought year in Derby compared to high counts in a much wetter year. This is in contrast to the analysis of grass pollen by Emberlin et al. (1999), which demonstrated earlier start dates but declining annual counts and severity, an effect that was attributed to changes in land use patterns such as declining agriculture and pasturelands. However, it is not clear if this explanation is also consistent with increasing trends in mold counts observed by Cordon and Millington (2001), who note that bursts of *Alternaria* follow grass mowing and harvest time. Hollins et al. (2004) found that summer temperature was the strongest projector of the number of days that *Cladosporium* spore concentrations exceeded 4,000 spores/m³, while there was a negative relationship between precipitation and spore counts.

In Tulsa, Oklahoma, Troutt and Levetin (2001) attempted to correlate fungal spore concentrations with meteorological data during May 1998 and May 1999. These 2 months were selected because they represented climatic extremes—May 1998 was exceptionally dry, and May 1999 had unusually high precipitation. The spore types studied were *Cladosporium*, *Alternaria*, *Epicoccum*, *Curvularia*, *Pithomyces*, *Drechslera*, smut spores, ascospores, and basidiospores. Dry air spora (i.e., *Cladosporium*) were much more prevalent during May 1998 (the dry year). No single multiple regression model successfully projected all spore concentrations, but temperature and dew point were important indicators.

Recent cyclic and extreme weather events have also been implicated in increased mold production. Research in New England found maximum mold counts to be higher and 2 to 4 weeks earlier after the occurrence of an El Niño event (Freye and Litwin, 2001). An examination of New Orleans housing stock after Hurricane Katrina revealed extensive mold growth (Ratard et al., 2006). The CDC assessed the extent of mold growth in a sample ($N = 112$) of households in the area. Almost half the homes had “visible mold growth,” and 17% had “heavy mold coverage,” defined as “>50% coverage on [the] interior wall of most-affected room.” Indoor and outdoor air sampling indicated *Aspergillus* spp. and *Penicillium* spp. were the predominant populations (Ratard et al., 2006). To the extent that extreme storm events such as Katrina are more likely to occur or more severe in the future due to climate change, poststorm mold problems may increase.

In summary, there is limited, but inconsistent evidence of increasing trends in mold production. Short-term forecasts indicate that while temperature and humidity can be strong predictors of mold concentrations, the effect varies by mold species and geography. At least one United States study observed an upward trend in *Cladosporium* but not for co-occurring mold such as *Alternaria* or *Epicoccum*. Another U.S. study observed increases in mold counts after an El Niño event, while in the U.K., an analysis showed increasing trends in *Alternaria*. After Hurricane Katrina, large portions of the housing stock were shown to have extensive mold growth (Ratard et al., 2006). Overall, the relationship between climate factors and mold species, extent, and geography suggests a complex multifactor mechanism. To the extent that extreme storm events such as Katrina are more likely or more severe in the future, due to climate change, poststorm mold problems may increase.

4.2. DISTRIBUTION OF AEROALLERGENS

Long-term responses to climate change (over 50 to 100 years) are likely to include changes in species' ranges or distributions. In some cases, extinction may occur. Generally, species are expected to migrate poleward and uphill as temperatures increase with climate change. The Bernard et al. (2001) evaluated continental level shifts in forest and vegetation distribution in the United States using various models and scenarios. Climate change scenarios were based on two atmospheric general circulation models (GCMs)—the Hadley model and the Canadian model. These models were selected because they represented the higher and lower halves of the range of temperature sensitivity among the GCMs available when the analysis was conducted. For both models, shifts in the distribution of vegetation types were projected with significant variation across geographic regions (Melillo et al., 2001). In studies of the fossil records in the United States, other researchers, Davis and Shaw (2001), project distribution shifts and extinctions based on extensive range shifts. In Europe, Emberlin (1994) also used computer models of future climatic changes resulting from increased CO₂ emissions and discussed the potential impact on the distribution of major allergenic pollen types.

Joyce et al. (2001) conducted a continental-scale analysis, for forest vegetation, of climate-induced changes in the distributions of biomes, community types, species richness, and individual tree and shrub species. Species interactions and the physiological response of species to carbon dioxide are not included in these models. The baseline scenario was the average climate for the 1961–1990 period. Comparisons were made to the transient Canadian and Hadley scenarios for the period 2070 to 2100. The results of these ecological models suggest that the potential habitats (i.e., distribution) for many tree species in the United States are likely to change, in some cases dramatically, by the end of the 21st century. Potential habitats for trees favored by cool environments are likely to shift northward. The habitats of alpine, subalpine spruce/fir, and aspen communities are likely to contract dramatically in the United States and largely shift into Canada. Potential habitats are likely to increase in the United States for oak/hickory, oak/pine, ponderosa pine, and arid woodland communities.

In a related review and analysis, Melillo et al. (2001) used biogeography model outputs to simulate shifts in the geographic distributions of major plant species by 2090–2099. The authors assume biogeochemical (i.e., production) changes will dominate ecological response to climate change in the next few decades, while species shifts will dominate by the end of the 21st century.

Unlike the models used for tree distribution, these models include CO₂ effects. Some of the major regional changes projected by the biogeography models for both Hadley and Canadian scenarios are as follows:

- *Northeast*: Forest will remain the dominant natural vegetation, but winter deciduous forest may expand at the expense of mixed conifer-broadleaf forest (Hadley). There could be a modest increase in savannas and woodlands (Canadian).
- *Southeast*: Forest remains the dominant natural vegetation, but the forest mix changes (Hadley). Alternatively, there could be significant expansion of savannas and grasslands at the expense of forest (Canadian).
- *Midwest*: Under both simulated climates (Hadley and Canadian), forest remains the natural vegetation, but the mix of forest types changes.
- *Great Plains*: Two of three models project an increase in woodiness, while one (Hadley) does not. The Canadian model suggests no change or a slight decrease in woodiness.
- *West*: Forest ecosystems grow at the expense of desert ecosystems (Hadley and Canadian).
- *Northwest*: Forest area grows slightly (Hadley and Canadian).

How well plants and trees actually track changes in potential habitats will be influenced by their dispersal abilities and disturbances in their environments. Davis and Shaw (2001) note that changes in geographic distribution are so frequently documented in the fossil record that range shifts are seen as the expected plant response to future climate change. These authors use fossil records of trees and cite evidence of genetic adaptation to climate to argue that the interplay of adaptation and migration has been central to the botanic response to climate change. The authors conclude that unprecedented rates of climate change anticipated to occur in the future, coupled with land use changes that impede gene flow, could result in extinctions of many taxa (see Figure 4-2). The complexity of range shifts is evidenced in a study of the observed increase in *Juniperus occidentalis* (Western Juniper) and coincident decrease in two herbaceous species in central Oregon, which the researchers did not find to be influenced by variability in climate, fire, grazing, or pathogens individually; however, they cannot exclude the cumulative effects of a favorable climate, decline in fire frequency, or increases in CO₂ concentrations as contributing to the observed land-cover change (Knapp and Soule, 1998).

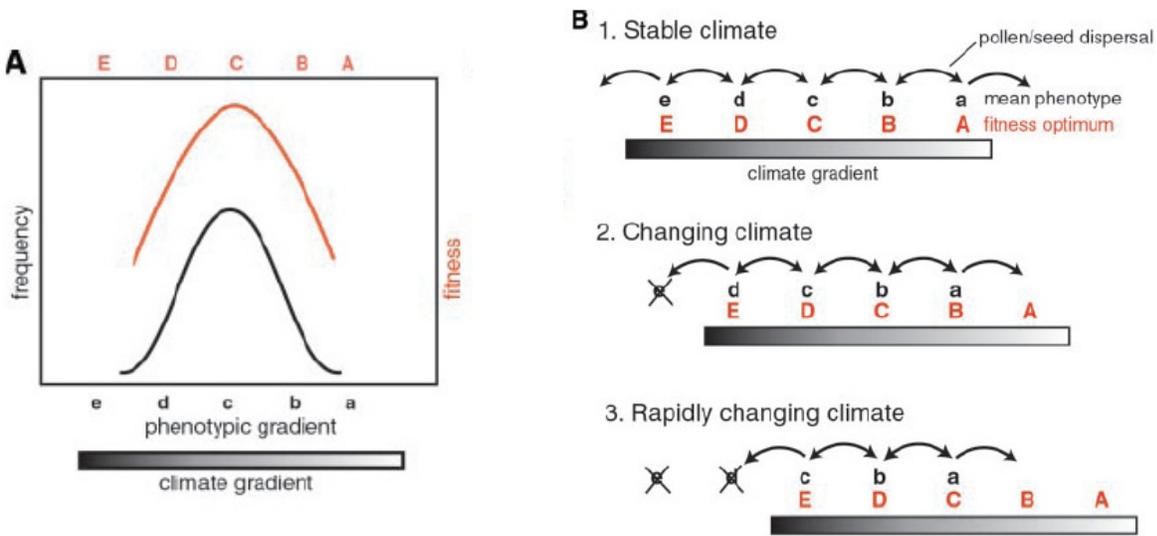


Figure 4-2. (A) Schematic depiction of phenotypic frequencies (mean phenotype) for a population at a location along a climate gradient where fitness maximum is C. (B) Schematic depiction of fitness optima (red) for a species that ranges across a climate gradient.

Notes: Adaptive differentiation of population phenotypes is shown in black; arrows indicate gene flow through pollen and seed dispersal. Spatial distributions of the climate gradient, fitness optima, and phenotypic frequencies are shown for three conditions: 1, stable climate; 2, slowly changing climate; and 3, rapidly changing climate.

Source: Davis and Shaw (2001, Figure 5).

Other research has relied on computer model projections of future climatic changes resulting from increased CO₂ emissions to gauge the potential impact on the distribution and abundance of major allergic pollen types in Europe (Emberlin, 1994). The results suggest an extension of the northern limit of birch by several hundred kilometers and a corresponding increase in height of the altitudinal tree line and contraction of the range in the south. Emberlin indicates that olive trees and ragweed could also experience a northward expansion.

In summary, long-term responses to climate change (over 50 to 100 years or more) are likely to involve range or distribution shifts in species, with possible extinction in some cases. Trees favoring cool environments, such as maple and birch, are likely to shift northward out of the United States entirely, thus dramatically altering the pollen distribution associated with them.

Under certain scenarios, the Southeast will experience significant warming trends, leading to an expansion of savannas and grasslands at the expense of forest, again altering the presence of major aeroallergens in large regions of the country.

4.3. DISPERSAL

There has been only limited research on how climate change could affect the dispersal of pollen and mold. However, there are cases of both pollen and dust being dispersed long distances from their release sites. For example, long distance dispersion of *Juniperus ashei* pollen has been routinely observed in Tulsa, Oklahoma (Van de Water et al., 2003). The nearest upwind sources of *J. ashei* pollen are 200 to 600 km from their deposition site (Tulsa). Analysis of the statistical relationship between wind direction and ragweed pollen counts in Pistoia and Florence, Italy, where ragweed plants do not grow, indicates that these pollen grains likely are the result of long distance transport from southern Hungary (Cecchi et al., 2006). Emberlin (1994) suggests that in Europe, increased strength of westerly winds due to climate change will enhance the long-range transport of birch pollen already observed to take place from north and central Europe to Scandinavia. Transcontinental transport of dust particulates has also been observed (Husar et al., 2001). Griffin et al. (2001) found *Cladosporium cladosporioides* in a sample of African dust in the air over St. John in the Virgin Islands, and Griffin et al. (2006) found various fungi species, some of which are associated with allergic diseases, in samples taken of the mid-Atlantic atmosphere believed to come from African desert dust. Additionally, many genera of fungus, including *Cladosporium*, *Alternaria*, *Penicillium*, and *Aspergillus* were found in air samples taken over Barbados in 1996–1997 of long-range transport dust from Africa (Prospero et al., 2005). During April 1998, two large dust storms occurred over the Gobi desert (Mongolia and north central China). The dust plume crossed the Pacific Ocean and resulted in strong spikes in particulate matter concentrations 10 days later (April 29) along the west coast of the United States (Husar et al., 2001). To the extent that climate change results in altered wind patterns and increased extreme weather events, one might expect corresponding changes in dispersion patterns of pollen and mold.

4.4. ALLERGEN CONCENTRATION

Allergic symptoms are related to pollen in a dose-response manner (Singer et al., 2005). While pollen concentration has been taken as the indicator of potential dose, the underlying mechanism for allergic symptoms comes in part from the protein allergens (antigen) in the pollen (Singer et al., 2005; Ahlholm et al., 1998; Beggs, 1998). Recent research has examined the influence of meteorological variables such as temperature and precipitation and air pollutants, such as carbon dioxide levels, on the concentration of allergen protein, or the allergenicity of pollen produced by ragweed and birch. The major allergen proteins in ragweed and birch are AMB A 1 (Antigen E) and BET V 1, respectively.

Using controlled environmental chambers, Singer et al. (2005) evaluated how AMB A 1 allergen concentrations changed in response to rising carbon dioxide concentrations. The authors used an enzyme-linked immunosorbent assay to quantify AMB A 1 in protein extracted from pollen of *A. artemisiifolia* grown at different CO₂ concentrations in a previous experiment. The CO₂ concentrations were 280, 370, and 600 µmol/mol. A key finding was that, while total pollen protein remained unchanged, AMB A 1 concentrations increased as a function of CO₂ concentrations. Relative to pollen grown at current CO₂ concentrations (i.e., 370 µmol/mol), pollen grown at 700 µmol/mol of CO₂ contained 1.6 times more AMB A 1 allergen ($p < 0.01$). The authors note that recent and projected increases in CO₂ concentrations could directly increase the allergen concentrations in ragweed pollen, and consequently, the prevalence and/or severity of seasonal allergic disease. They also point out, however, that genetic and abiotic factors governing allergen expression will need to be better established to fully understand these data and their public health implications.

Ahlholm et al. (1998) investigated the impact of genetics and temperature on the allergen content of birch (*B. pubescens*) pollen by studying trees of 10 half-sib families. Pollen samples were collected from two tree line gardens where the daily mean temperatures were different during the growing season due to altitudinal differences between the gardens. The temperature difference was approximately 1.0 to 2.5°C. After controlling for descendant group, the authors found that IgE-immunoblotting responses were stronger in sera exposed to pollen grown at the higher temperature. It is unclear whether the effect originated during the previous or the current growing season. Differences in allergen concentration were also seen between different

progenies of trees. The authors suggest the lower soil temperature, which limits nutrient (i.e., nitrogen) uptake and, thus, the rate of allergen synthesis, as a possible mechanism.

The research on allergen content of pollen/mold is limited but does suggest that even if pollen production remained unchanged, allergic illness could increase due to increasing levels of allergenic protein within pollen grains.

4.5. CLIMATE VARIABILITY AND ALLERGIC DISEASES

Climate change caused by elevated greenhouse gases, including carbon dioxide, is expected to lead to increases in global mean temperature, a stronger hydrologic cycle, and an increase in the number and severity of extreme weather events. These changes may lead to alterations in the production, distribution, and dispersion of aeroallergens, as well as changes in allergen protein concentration. It is possible that production (both timing and amount) and protein content of aeroallergens will increase, and with time, plant distributions will shift as well. If changes in aeroallergen production occur as a result of climate change, then the patterns of seasonal allergic disorders, such as allergic rhinitis (hay fever), asthma, and possibly atopic dermatitis could be affected as well.

The development of allergic illness is a multistage process in which a genetically predisposed and immunologically naïve individual is first sensitized to an allergen, resulting in the production of IgE antibodies (Nielsen et al., 2002), and then subsequent exposures elicit a disease response due to the presence of IgE antibodies and the associated cellular response. Furthermore, there appears to be a dose-response relationship between allergen exposure, sensitization, and exacerbation of disease (Nielsen et al., 2002). Thus, there are at least three causal pathways for climate change-induced impacts on aeroallergens to alter the severity and possibly the prevalence of allergic diseases. First, a longer exposure during sensitization may lead to greater likelihood of the development of allergy (increased prevalence). Second, a higher dose during sensitization may lead to a greater likelihood of development of an allergy (increased prevalence). Third, a higher dose during subsequent exposures (postsensitization) may lead to a more severe allergic response (Nielsen et al., 2002). Figure 4-3 outlines this process using asthma as an example (Beggs and Bambrick, 2005).

Definitive statements on the impact of climate change on aeroallergens and subsequent allergic illness, however, are rarely found in the literature. This is in part because studies are of

necessity often narrowly defined, and a single study is unlikely to encompass the broad subject of weather, aeroallergens, and allergic illness. There is also an inherent uncertainty as to how the climate will change, especially at a regional level. The etiology of allergic diseases, especially asthma, is complex and has a gene-environment interaction that is poorly understood. In addition, there are numerous other factors that come into play, such as changes in land use, air pollution, adaptive responses, and modifying factors that are difficult to assess (see Figure 4-4). The interaction between atmospheric pollutants and aeroallergens adds a further complication, as there is evidence of mediating effects of air pollution on the allergic responses in exposed individuals (D'Amato et al., 2002). However many studies of the health effects of air pollutants do not take into account the possible confounding, synergistic, or antagonistic effect of aeroallergens. It is important that more studies, particularly ones investigating the role of air pollution on asthma exacerbations, take into account aeroallergens to further understanding of this complex interaction.

This section reviews the evidence and provides a qualitative assessment of the likely impact of climate change on allergic illnesses based on the expected changes in production, distribution, and dispersion of aeroallergens and allergen content of aeroallergens in response to climate change. It then reviews a limited number of studies on weather, aeroallergens, and allergic disease.

4.5.1. Timing of Aeroallergen Production and Subsequent Illness

Shifts in phenology are one of the most consistent findings in studies of plant pollen production (Root et al., 2003). Alterations in the timing of aeroallergen production in response

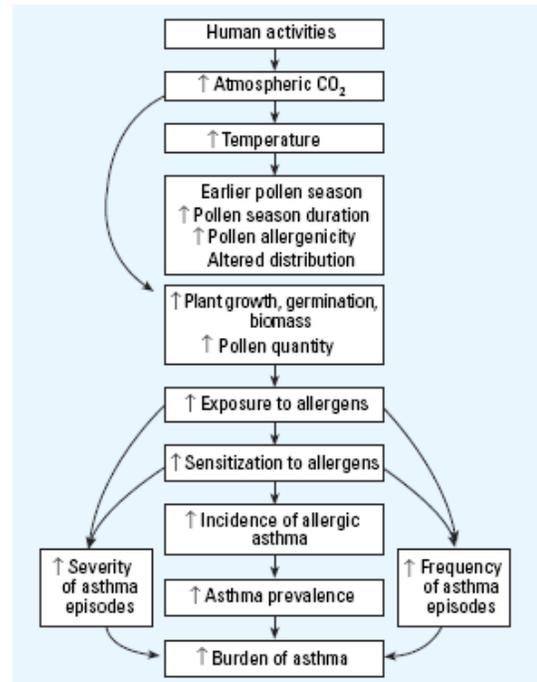


Figure 4-3. Schematic diagram of the relationship between global climate change and the rise in asthma prevalence and severity, via impacts of climate change on plant and pollen attributes.

Source: Beggs and Bambrick (2005, Figure 4).

to weather variables have been clearly demonstrated for certain tree species, but less so for grass and weed pollens and mold (Clot, 2003; Emberlin et al., 2002; Katial et al., 1997). This is consistent with the observation that the flowering of many trees is regulated by temperature, whereas photoperiod determines the flowering of many weeds in late summer. Evidence is mixed for grass pollens, with trend studies showing substantial differences by region in England (Emberlin, 1994), earlier start dates in Switzerland (Clot, 2003), but no apparent effect after an El Niño event in New England (Freye and Litwin, 2001).

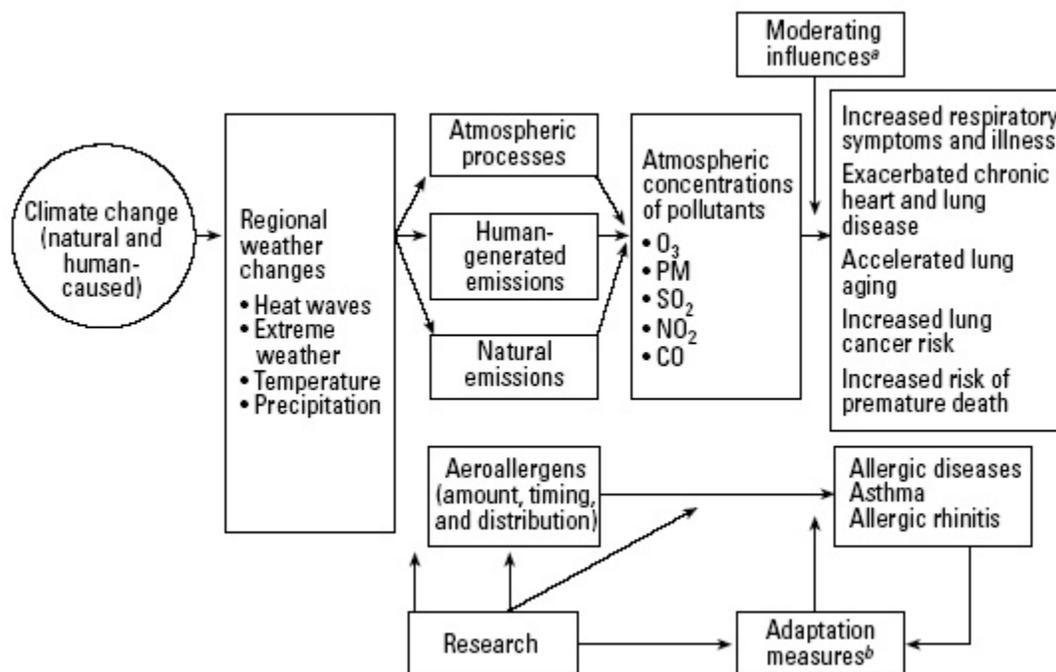


Figure 4-4. Potential air pollution-related health effects of climate change.

Notes: ^aModerating influences include nonclimate factors that affect climate-related health outcomes, such as population growth and demographic change, standards of living, access to health care, improvements in health care, and public health infrastructure.

^bAdaptation measures include actions to reduce risks of adverse health outcomes, such as emission control programs, use of weather forecasts to project air quality levels, development of air quality advisory systems, and public education.

Source: Bernard et al. (2001, Figure 1).

Ragweed has been shown to flower earlier in urban environments where temperature and CO₂ concentrations were higher compared to rural areas (Ziska et al., 2003). There was limited evidence on the start dates for the emergence of mold, although the El Niño event in New England indicated an earlier start (Freye and Litwin, 2001). Some mold such as *Alternaria* is associated with agriculture, and therefore, the timing of production will be associated with the harvest (Corden and Millington, 2001). The concentrations of indoor allergens (e.g., dust mites, cockroaches) do not vary seasonally.

Analyses of trends in allergenic illness, however, are based on annual prevalence and generally do not document the seasonal timing of these illnesses within the year. Nevertheless, in sensitized individuals, exposure clearly leads to allergic response; thus, it is reasonable to expect that changes in the timing of production of seasonal aeroallergens would result in corresponding changes in the timing of the associated seasonal allergenic illness (i.e., rhinitis). There is not clear evidence that the timing of mold emergence has shifted, and indoor allergens are generally not seasonal. In addition, the relationship between indoor allergens and climate change is unclear. Shifts in the timing of asthma and atopic dermatitis in response to changes in phenology are not as predictable.

4.5.2. Aeroallergen Production, Allergen Content, and Subsequent Illness

Increases in aeroallergen production and/or protein concentration could impact the prevalence or severity of allergic illness via sensitivity and response pathways. A key conclusion of the NAST (Melillo et al., 2001) was that over the next few decades, climate change is likely to lead to increased plant productivity and carbon storage for many parts of the country, especially those areas that become warmer and wetter. Therefore, pollen production and possibly mold (e.g., *Cladosporidium*) in these areas would be expected to increase, on average. The NAST also concluded that areas where soils dry out during the growing season, such as the Southeast under certain scenarios, are likely to see reduced productivity and carbon storage, and hence, less pollen production.

These conclusions are supported by experimental and field studies that have demonstrated increased pollen production in ragweed and other species in conditions similar to those expected with climate change (Ziska et al., 2003, Jablonski et al., 2002; The Center for Health and the Global Environment, 2005). There are several examples where regional weather

patterns, i.e., increased precipitation and temperature, lead to stronger pollen production (Freye and Litwin, 2001; Reiss and Kostic, 1976; Weber, 2003a, b). One study conducted in the United States showed increasing trends of total pollen production in cedar, oak, hickory, pecan, and birch in Oklahoma that may have been attributable to warmer winters (Levetin, 2001). In addition, studies of birch and ragweed provide evidence of increasing allergen content under similar conditions.

However, while the prevalence of both hay fever and asthma have increased in recent years (see Section 3.2), the limited observational data on aeroallergen trends in the United States present some difficulty in making an association to the observed increases in these allergic diseases. While there is at least one regional example of increasing trends in mold (Katial et al., 1997) and tree pollen (Lapidus, 2001), the observational studies of United States pollen levels do not appear to have sufficient data (i.e., >10 years) to conduct trend analyses. The increases in allergen content observed in experiments, however, may provide an alternative explanation for increasing allergic illness prevalence in the absence of documented increases in pollen levels.

On the basis of model projections by the NAST, pollen production in many areas of the country may increase until mid-21st century. It is also possible but less clear if allergen content and mold production may increase as well. Exposure to elevated pollen and mold concentrations during sensitization may lead to a greater likelihood of development of an allergy such as rhinitis or asthma—i.e., the prevalence of allergic disease might increase. In addition, exposures to higher concentrations of aeroallergens or allergen proteins may lead to more severe allergic responses (Nielsen et al., 2002; Singer et al., 2005). It is unclear how indoor allergen concentrations might change, but there may be changes in exposure patterns. For example, more time could be spent indoors during summer heat waves, but less time could be spent indoors during the winter as minimum temperatures rise (Patz et al., 2000).

These inferences are similar to the findings of a recently published report, *Climate Change Futures*, sponsored by Swiss Re and the United Nations Development Programme and conducted by The Center for Health and the Global Environment at Harvard Medical School. The Climate Change Futures (CCF) project relied on two scenarios of gradual warming with growing variability and more weather extremes. These scenarios were then applied to case studies, one of which included asthma. Both scenarios are based on business-as-usual, which, if unabated, would lead to a doubling of atmospheric CO₂ concentrations by the mid 21st century.

The first impact scenario (CCF-1) is based on gradual warming, with increasing variability and escalating impacts. The second impact scenario (CCF-2) is also based on gradual warming with increasing variability but includes surprise impacts due to abrupt climate change. The CCF-1 envisions a perceptible impairment of public health as a result of higher concentrations of aeroallergens whether measured by morbidity and mortality, disability adjusted life years (DALY)¹¹ lost, or the value of the incremental medical resources devoted to the emerging medical problems. The CCF-2 suggests that the combination of more aeroallergens, more heat waves, photochemical smog, greater humidity, more wildfires, and more dust and particulates could considerably compromise respiratory and cardiovascular health in the near term. Widespread respiratory distress is plausible for large parts of the world, bringing with it increasing disability, productivity losses, school absences, and rising costs for health care and medications.

Ecological models indicate climate change will likely lead to increased plant productivity and carbon storage in many parts of the country. Experimental and observational analyses support model assessments, but production changes may be species- and region-specific. Data gaps limit assessment of trends in United States pollen and mold. Increases in aeroallergen production and/or allergen content could lead to increased prevalence and severity of allergic diseases. A recent report by Harvard Medical School envisions perceptible impairments in public health as a result of higher concentrations of allergens due to climate change (The Center for Health and the Global Environment, 2005).

A study in Genoa, Italy observed that the total yearly pollen counts for *Parietaria* pollen significantly increased from 1981 to 1997 but that pollen sensitivity in the population did not show much year-to-year variability. However, sensitivity to *Parietaria* was highest in the population living in the area where *Parietaria* had the highest pollen count of the pollens studied. For the other pollens they studied, counts of Poaceae and *Artemisia* did not show any significant upwards trends, and while *Ambrosia* pollen counts have been increasing during the time period studied, very few people are sensitized to it, which could be attributed to its low overall count compared to the other pollens studied (Voltolini et al., 2000).

¹¹DALY = The sum of years of potential life lost due to premature mortality and the years of productive life lost due to disability.

4.5.3. Distribution and Dispersion of Aeroallergens and Subsequent Illness

Changes in the geographic distribution of plants and mold may alter the distribution of allergic illness. Long-term responses to climate change (over 50 to 100 years) are likely to involve range or distribution shifts in species and, in some cases, extinction of species (Joyce et al., 2001; Melillo et al., 2001; Davis and Shaw, 2001). The results of ecological models indicate that the potential habitats (i.e., distribution) for many tree species in the United States are likely to change, in some cases dramatically, by the end of the 21st century. Potential habitats for trees favored by cool environments are likely to shift northward (Joyce et al., 2001). The habitats of alpine, subalpine spruce/fir, and aspen communities are likely to contract dramatically in the United States and largely shift into Canada. Potential habitats are likely to increase in the United States for oak/hickory, oak/pine, ponderosa pine, and arid woodland communities. Projections for (nonforest) vegetation redistribution suggest that savannahs and grasslands are likely to expand, especially in the Southeast, where hot and dry climate conditions are projected in response to climate change.

The models developed for the NAST are supported by fossil record evidence. Davis and Shaw (2001) note that changes in geographic distribution are so frequently documented in the fossil record that range shifts are seen as the expected plant response to future climate change. These authors cite evidence of genetic adaptation to climate and argue that the interplay of genetic adaptation and migration has been central to the biotic response to climate change.

Assessing the potential impact of vegetation range shifts on allergic illness is difficult. Shifts in vegetation distribution are likely to occur over relatively long periods of time, i.e., decades. Furthermore, cross-reactivity between species implies that the range of a species (e.g., birch) could contract or move northward and another (e.g., white oak) could take its place without any appreciable difference in allergic illness. However, one can look to examples of invasive and cultivated species to assess the potential impacts on allergic illness. Ragweed, for example, has spread throughout Europe in recent decades and is now regarded as a major allergen in France, north Italy, Hungary, and Croatia (Stefanic et al., 2005) and is beginning to spread into Switzerland (Taramaraz et al., 2005). Pollen counts for ragweed are increasing in Europe as are the number of people allergic to ragweed in Hungary, northern Italy, the Rhone area of France, Prague and Brno in the Czech Republic, and Vienna, Austria (Rybnicek and Jaeger, 2001); however, no statistical link was made between the pollen counts and prevalence of

ragweed allergy. In desert regions such as the southwestern United States, the natural vegetation is primarily animal- or insect-pollinated (Sneller et al., 1993). However, urban development and landscape preferences for grasses and shade trees (i.e., wind-pollinated plants) in areas such as Tuscon, Arizona have led to dramatic changes and increases in the pollen burden (Sneller et al., 1993).

There is some indication that the introduction of new pollens into a region can lead to increased allergic illnesses in the population, even among people who did not have prior allergies to other pollens. The increase in pollen allergies to birch and ragweed pollens has been attributed to the introduction of birch trees into the suburbs north of Milan in the 1970s and 1980s and the natural spread of ragweed into the area in the 1980s, and an investigation into people with new allergies solely to birch or ragweed pollen found that they had an older age of onset of allergies and were less likely to have a family history of allergic illnesses compared to people allergic to other pollens naturally found in the area (Asero, 2002).

There has been only limited research on how climate change could effect the dispersal of pollen and mold. Dispersion has the potential via shifts in long-term weather patterns and extreme weather events to expose human populations (sensitize) to novel allergens and to create severe and possibly life threatening exposures. There are cases of both pollen and dust being dispersed long distances from their release sites. For example, long distance (200–600 km) dispersion of *Juniperus ashei* pollen has been routinely observed in Tulsa, Oklahoma and is associated with allergic illness in that community (Van de Water et al., 2003). Transcontinental transport of dust particulates has also been observed (Husar et al., 2001). During April 1998, two large dust storms occurred over the Gobi desert (Mongolia and north central China). The dust plume crossed the Pacific Ocean and resulted in strong spikes in particulate matter concentrations 10 days later (April 29) along the west coast of the United States (Husar et al., 2001). It is unclear if there were any health impacts associated with the dust in the United States, but state health agencies issued air pollution advisory warnings to the general public (Husar et al., 2001).

In summary, shifts in vegetative distribution are expected to occur but over relatively long periods of time. There does not appear to be any literature estimating the impact of climate change on the distribution of aeroallergens and subsequent illness. The impact of climate change on aeroallergen dispersion and subsequent illness does not appear to be well studied either.

There are specific examples of dispersion, indicating that exposure to novel aeroallergens or unusually high concentrations of allergens are distinct possibilities. Overall, however, it is difficult to project how changes in dispersal patterns and geographic distribution of plants and mold may impact allergic illness.

4.5.4. Observational Studies of Weather, Aeroallergens, and Illness

There are several examples of observational studies that provide a linkage between weather, aeroallergens, and health outcomes. These studies provide limited evidence of the seemingly obvious but difficult to demonstrate link between weather, aeroallergen production, and subsequent illness. A study by Epton et al. (1997) is one of the few examples of a prospective design that integrates the three variable categories (i.e., weather, aeroallergens, illness) and can serve as a model for future studies.

Epton et al. (1997) conducted a 1-year prospective study to explore relationships between weather, fungal spore counts, pollen counts, and peak expiratory flow rates (PEFRs) and asthma in a group of asthmatic subjects. A small positive association was found between PEFR and mean temperature. The study also found an association between days with high basidiospore counts and nocturnal waking and medication use to relieve asthma. The authors concluded that the effects of weather and aeroallergens on PEFR and asthma symptoms in the studied population were small and that other causes needed to be sought out to explain variations in asthma severity and exacerbations. However, there were no control subjects, and 75% of the cases were users of prescribed inhaled anti-inflammatory medications—usually corticosteroids. Steroid use combined with the low to moderate pollen levels during the study may explain why the authors did not find a more substantial role of aeroallergen influence on asthma.

A time-series study of the link between grass and weed pollen and emergency department (ED) visits for asthma in Montreal found that significant increases in grass pollen concentrations corresponded to increases in first time ED visits for asthma with a lag of 3 and 5 days, whereas readmissions for asthma increased 4 days after an increase in grass pollen concentrations. Adding meteorological or air pollution variables, however, did not significantly affect the relationships found between pollen and asthma (Heguy et al., 2008).

Another study in Montreal investigated the links between weather, *Ambrosia* (ragweed) pollen, and medical consultations for allergic rhinitis. *Ambrosia* pollen concentrations were

significantly positively correlated with maximum, mean, and minimum temperatures but negatively correlated with precipitation. The authors analyzed the number of over-consultations each day, defined as the number of consultations greater than the average for that day of week during pollen season, with *Ambrosia* pollen concentrations while controlling for meteorological variables and pollen season. Logistic regression showed strong correlations between pollen count and over-consultations for allergic rhinitis on the day of high pollen exposure as well as 1, 2, 3, and 5 days after high pollen exposure (Breton et al., 2006).

Lewis et al. (2000) investigated the joint effects of aeroallergens, rainfall, thunderstorms, and outdoor air pollutants on daily asthma admissions and Accident and Emergency (A&E) attendance using routinely collected data between 1993 and 1996 in Derby, England. The authors found a significant interaction between the effects of grass pollen and weather conditions on A&E attendance, such that the increase in attendance with grass pollen count was most marked on days of light rainfall. Asthma admissions also increased significantly with *Cladosporium* count.

Severe weather events also provide intriguing evidence of an association between weather, aeroallergens, and allergic illness. Dales et al. (2003) explored the hypothesis that thunderstorms, by increasing aeroallergen levels, cause exacerbations in asthma. The analysis was done using 6 years of emergency department visit data with approximately 4,000 asthma hospital admissions yearly. Air pollution, meteorological factors, and aeroallergen levels were accounted for simultaneously. The authors found an average daily rate of 8.6 asthma visits on days without thunderstorms and a 15% increase to 10 visits ($p < 0.05$) on days with thunderstorms. The concentrations of total fungal spores almost doubled during thunderstorms (from 1,512 to 2,419 m^3). A time series analysis was used to test the association between changes in daily concentrations of aeroallergens and changes in the daily number of emergency visits irrespective of thunderstorms; there was a significant association with fungal spores but not pollen. Air pollution was also higher on days with thunderstorms compared to days without, but the time series analysis detected no significant effect of these pollutants (O_3 , SO_x , NO_x , haze) on asthma.

Analysis of cases of asthma hospital admissions during a thunderstorm compared to asthmatic controls found that there were high correlations between the timing of the thunderstorm, concentrations of *Didymella*, *Cladosporium*, and broken *Alternaria* spores, and

asthma hospital admissions. They also found that the odds of being sensitive to either *Alternaria* and/or *Cladosporium* spores was significantly increased for the thunderstorm-induced asthma admissions compared to controls (Pulimood et al., 2007).

Hurricane Katrina provides a recent example of extreme weather in the United States and the potential impact on aeroallergens and allergic illness. Large sections of New Orleans were flooded for weeks, resulting in extensive mold growth in buildings. The CDC assessed the extent of mold growth in a sample ($N = 112$) of households in the area (Orleans, Jefferson, Plaquemines, and St. Bernard Parishes) and collected indoor ($N = 20$) and outdoor ($N = 11$) air samples. Almost half the homes had “visible mold growth,” and 17% had “heavy mold coverage,” defined as “>50% coverage on [the] interior wall of most-affected room” (Ratard et al., 2006). Indoor and outdoor air sampling indicated *Aspergillus* spp. and *Penicillium* spp. were the predominant populations (Ratard et al., 2006). Geometric mean glucan levels were $1.6 \mu\text{g}/\text{m}^3$ inside homes and $0.9 \mu\text{g}/\text{m}^3$ outside. Geometric mean endotoxin levels were $23.3 \text{ EU}/\text{m}^3$ (endotoxin units per cubic meter) inside and $10.5 \text{ EU}/\text{m}^3$ outside. Solomon et al. (2006) also took indoor ($N = 8$) and outdoor ($N = 23$) mold samples in October and November 2005 in New Orleans and found that the main mold spores found in outdoor air were *Cladosporium*, *Aspergillus*, and *Penicillium* species, whereas indoors, more than 70% of the identified spores were *Aspergillus* and *Penicillium*. Their samples showed much higher spore concentrations in outdoor flooded areas (mean = $66,167 \text{ spores}/\text{m}^3$) compared to unflooded areas (mean = $33,179 \text{ spores}/\text{m}^3$), which were also higher than the background spore concentration for the region (mean = $23,835 \text{ spores}/\text{m}^3$), and that inside spore concentrations (mean = $320,005 \text{ spores}/\text{m}^3$) were higher than concentrations just outside. The authors also found that homes that had been partially or fully remediated for mold had lower spore concentrations than the homes that had not been touched since the flooding. They found no appreciable difference in endotoxin concentrations for flooded and unflooded areas.

Hospitals in the area have reported seeing an increased number of patients with allergy and cold symptoms, and doctors have suggested that allergy to the mold and dust circulating in New Orleans is making residents susceptible to respiratory illness (Wilson, 2006). There are also reports of a nagging cough throughout New Orleans that has been nicknamed “Katrina cough,” believed to be caused by high levels of “dust” in the air—particles from construction debris and dried mud, coupled with high spore counts from mold and mites that feed on mold

spores (Bennett, 2006). This a particular concern for workers removing debris (Wilson, 2006). Overall rates of asthma in Louisiana children have also increased post-Katrina from 14% (2003) to 18% (2006) according to results from the Louisiana Child & Family Health Study, and may be even higher for minority and underprivileged children or children residing in certain geographical areas that were affected by post-Katrina flooding (The Center for Health and the Global Environment, 2005).

Studies examining the relationship between weather, aeroallergens, and health outcomes, provide intriguing evidence of potentially serious impacts on health. For example, asthma prevalence is reportedly higher in post-Katrina Louisiana; spikes in mold spore concentrations and asthma have been observed on days with thunderstorms. Additionally, light rain and grass pollen counts were associated with asthma admissions in the United Kingdom. However, for diseases with complicated etiologies, such as asthma, more rigorous prospective designs as conducted by Epton et al. (1997) may be required to better understand the relationship between weather, aeroallergens, and illness.

4.5.5. Linkages Among Air Pollution, Aeroallergens, and Allergic Diseases

Some recent studies have shown that the links between air pollution, aeroallergens, and allergic diseases are complex and that air pollution may play a significant role in the etiology of some allergic diseases. D'Amato et al. (2002) hypothesize that the reason for the increase in urban allergic disease could be due to the role that air pollutants play in mediating the health effects of aeroallergens. The authors summarize the literature that demonstrates that the inflammatory effects of ozone, particulate matter, and sulfur dioxide allow for easier penetration of pollen allergens into the airways, that air pollutants can increase the release of antigens in pollen grains that lead to allergic responses, and that pollutants can also absorb pollen grains and, thus, prolong their retention in the body. Given that climate change may increase temperature-dependent air pollutants as well as aeroallergens, the interactions between criteria air pollutants and aeroallergens are important for further study.

Knowlton et al. (2007) mapped the locations of ragweed pollen prevalence and the areas with at least one ozone exceedance day per year on the same map of the United States, thereby indicating the locations where people would be at an increased risk of asthma symptoms from two sources known to affect asthma. Notably, 14 of the 15 cities listed by the Asthma and

Allergy Foundation of America as the “most challenging places to live with asthma” fell in areas that had overlapping risks of ozone and ragweed. These regions of overlap also highlight regions of future vulnerability, given that both ragweed prevalence and ozone levels are projected to increase with climate change.

In observational studies of asthma, where aeroallergens and air pollutants could both be the cause, it is important that analysis be done on the potential for confounding of one by the other. Of the few studies that have investigated such confounding, differing results have been found, which may be due to the statistical methods used, the location of the study, or other factors. For example, in a study investigating the link between air pollution and emergency department visits for asthma in Alberta, Canada, the researchers found that adding aeroallergen data to their time stratified case-crossover study design did not change their risk estimates for air pollution’s effects on ED visits for asthma (Villeneuve et al., 2007). However, a study focusing on the relationship between grass pollen and ED visits for asthma in Melbourne, Australia found that the air particle index and NO₂ were independently associated with asthma ED visits but that grass pollen was still associated with asthma ED visits even with all of the air pollutants added to the model (Erbas et al., 2007). These are just two examples of studies that investigate the complex interactions of impacts of air pollutants and aeroallergens on respiratory health effects.

The interrelationships between climate variability, air pollution and aeroallergens are very complex, so that projections of climatic changes for any of these gets complicated by the lack of complete understanding and the many variables involved. A recent review of these issues by D’Amato and Cecchi (2008) explains this complexity and demonstrates how projected climate changes could have both positive and negative effects on respiratory allergies given the many multifaceted ways in which climate changes and other global changes of urbanization and increased energy uses may impact air pollutants, aeroallergens, and, therefore, allergic illnesses.

5. ECONOMIC AND QUALITY-OF-LIFE IMPACTS OF ALLERGIC DISEASES

This section of the report focuses on the costs, both monetized and nonmonetized, of allergic diseases. Unless stated otherwise, all costs are in 2005 dollars.¹² The incidence of allergic disease has grown substantially in recent years, affecting millions of people annually. Allergic reactions can involve several organ systems, including the respiratory tract, skin, cardiovascular system, and the gastrointestinal tract. A recent nationwide survey reported that 54.6% of people in the United States test positive for one or more common allergens (AAAAI, 1996–2005); among specific allergens, dust mite, rye, ragweed, and cockroach caused sensitization in approximately 25% of the population (Arbes et al., 2005). Allergies are the sixth most costly chronic disease category in the United States, costing the health care system approximately \$21 billion annually (AAAAI, 1996–2005).

Although there are several different types of allergic disease affecting the respiratory tract, skin, and other organ systems, this section discusses the costs of those allergic diseases that have been associated with common aeroallergens in the United States—primarily, allergic rhinitis/rhinoconjunctivitis (hereafter referred to as “allergic rhinitis”), asthma, and atopic dermatitis/eczema (hereafter referred to as “atopic dermatitis”). Table 5-1 shows nationwide hospital statistics for the conditions of interest.

The AAAAI reports that allergic rhinitis affects approximately 40 million people in the United States each year, 40% of whom are children. Estimated total direct costs of treatment are \$6.2 billion per year. Indirect costs include 3.8 million missed days of school and work per year. Allergic rhinitis seldom results in hospitalization. In 2003, the total number of hospital discharges with allergic rhinitis listed as the principal diagnosis was 293; the total number including those with allergic conjunctivitis in addition was 368. The aggregate charges totaled \$2.1–\$2.5 million (see Table 5-2 and Table 5-3). For the most part, direct medical costs of allergic rhinitis treatment can be attributed to outpatient services and medications (Schoenwetter et al., 2004).

¹²Medical costs were inflated to 2005 U.S. dollars using Bureau of Labor Statistics Consumer Price Index (BLS CPI) for Medical Care. All other costs were inflated to 2005 dollars using BLS CPI.

Table 5-1. National hospital statistics, 2003—principal diagnosis only (all conditions)

	Total number of discharges	LOS (length of stay), days (mean)	Mean hospital charge (2005\$)	Aggregate charges, (the "national bill") (2005\$)	Admitted from emergency department	In-hospital deaths
Asthma (ICD-9: 493)	469,738	3.4	12,623	5,931,347,575	338,659 (72.10%)	1,669 (0.36%)
Allergic rhinitis ^a (ICD-9: 477)	293	1.9	7,192	2,109,848	178 (60.90%)	0 (0.00%)
Allergic conjunctivitis ^b (ICD-9: 372.05, 372.13, 372.14)	75	2.1	5,629	420,298	45 (60.56%)	0 (0.00%)
Allergic rhinoconjunctivitis AR+AC	368	1.9	6,870	2,530,146	224 (60.83%)	0 (0.00%)
Atopic dermatitis/eczema ^c (ICD-9: 691.8 692.9 373.3)	2,582	3.2	9,163	23,801,038	1,550 (60.03%)	0 (0.00%)

^aAllergic rhinitis or AR.

^bAllergic conjunctivitis or AC (defining ICD codes adopted from (Ray et al., 1999).

^cDefining ICD codes adopted from (Ellis et al., 2002).

Notes: 2003 dollar values were inflated to 2005 dollars using BLS CPI for Medical Care.

Source: Weighted national estimates from HCUP Nationwide Inpatient Sample (NIS), 2003, AHRQ, based on data collected by individual states and provided to AHRQ by the states. Total number of weighted discharges in the United States based on HCUP NIS = 38,220,659. (<http://hcup.ahrq.gov/HCUPnet.asp>).

Table 5-2. Allergic rhinitis national hospital statistics, 2003—principal diagnosis only

		Total number of discharges	LOS (length of stay), days (mean)	Mean hospital charge, (2005\$)	Aggregate charges, (the "national bill") (2005\$)	Admitted from emergency department	In-hospital deaths
All discharges		293 (100.00%)	1.9	7,192	2,109,848	178 (60.90%)	0 (0.00%)
Age group	<1	*	*	*	*	*	*
	1–17	71 (24.17%)	1.6	5,948	420,884	41 (57.76%)	0 (0.00%)
	18–44	100 (34.29%)	1.8	7,372	740,138	58 (57.51%)	0 (0.00%)
	45–64	52 (17.93%)	2.8	*	*	24 (46.62%)	0 (0.00%)
	65–84	55 (18.90%)	1.6	6,855	379,407	46 (83.33%)	0 (0.00%)
	85+	*	*	*	*	*	*
Region	Northeast	89 (30.54%)	1.7	4,809	429,975	65 (73.04%)	0 (0.00%)
	Midwest	*	*	*	*	*	*
	South	133 (45.27%)	2.2	9,224	1,222,748	82 (61.64%)	0 (0.00%)
	West	*	*	*	*	*	*

Notes: 2003 dollar values were inflated to 2005 dollars using BLS CPI for Medical Care; ICD-9 code 477; statistics based on 70 or fewer unweighted cases in the nationwide statistics (NIS and KID) are not reliable. These statistics are suppressed and are designated with an asterisk (*).

Source: Weighted national estimates from HCUP Nationwide Inpatient Sample (NIS, 2003), Agency for Healthcare Research and Quality (AHRQ), based on data collected by individual states and provided to AHRQ by the states. Total number of weighted discharges in the United States based on HCUP NIS = 38,220,659 (<http://hcup.ahrq.gov/HCUPnet.asp>).

Table 5-3. Allergic rhinoconjunctivitis national hospital statistics, 2003—principal diagnosis only

		Total number of discharges	LOS (length of stay), days (mean)	Mean hospital charge, (2005\$)	Aggregate charges, (the "national bill") (2005\$)	Admitted from emergency department	In-hospital deaths
All discharges		368 (100.00%)	1.9	6,870	2,530,146	224 (60.83%)	0 (0.00%)
Age group	<1	*	*	*	*	*	*
	1–17	95 (25.71%)	1.6	5,311	501,866	45 (47.84%)	0 (0.00%)
	18–44	121 (32.80%)	1.8	6,894	831,111	78 (64.61%)	0 (0.00%)
	45–64	58 (15.87%)	2.7	9,225	530,748	30 (51.94%)	0 (0.00%)
	65–84	75 (20.52%)	2.1	7,688	579,817	56 (74.44%)	0 (0.00%)
	85+	*	*	*	*	*	*
Region	Northeast	114 (31.04%)	1.7	5,214	594,857	85 (74.51%)	0 (0.00%)
	Midwest	61 (16.72%)	1.4	4,231	260,040	31 (50.26%)	0 (0.00%)
	South	142 (38.56%)	2.3	9,142	1,295,354	86 (60.96%)	0 (0.00%)
	West	*	*	*	*	*	*

Notes: 2003 dollar values were inflated to 2005 dollars using BLS CPI for Medical Care; ICD-9 codes 477 (AR), and 372.05, 372.13, 372.14 (AC, see [Ray et al., 1999]); statistics based on 70 or fewer unweighted cases in the nationwide statistics (NIS and KID) are not reliable. These statistics are suppressed and are designated with an asterisk (*).

Source: Weighted national estimates from HCUP Nationwide Inpatient Sample (NIS, 2003), Agency for Healthcare Research and Quality (AHRQ), based on data collected by individual states and provided to AHRQ by the states. Total number of weighted discharges in the United States based on HCUP NIS = 38,220,659 (<http://hcup.ahrq.gov/HCUPnet.asp>).

Asthma is estimated to affect approximately 15 million Americans (AAAAI, 1996–2005). The condition often begins in childhood, and it has been estimated that 30% of all patients are children. There were 1,669 deaths due to asthma in 2003 (see Table 5-4). The age-adjusted death rate for asthma has been in the neighborhood of 5 deaths per 100,000 during the past decade (see Figure 5-1). In addition, asthma is indicated as a “contributing factor” for nearly 7,000 other deaths in the United States each year (NCHS/CDC, 2001). Asthma was given as the primary diagnosis in about 500,000 hospitalizations in 2003 and was listed as a secondary diagnosis in over 1 million hospitalizations (see Table 5-2).

Table 5-4. Asthma national statistics, 2003—principal diagnosis only

		Total number of discharges	LOS (length of stay), days (mean)	Mean hospital charge (2005\$)	Aggregate charges, (the "national bill") (2005\$)	Admitted from emergency department	In-hospital deaths
All discharges		469,738 (100.00%)	3.4	12,623	5,931,347,575	338,659 (72.10%)	1,669 (0.36%)
Age group	<1	16,631 (3.54%)	2.5	8,655	143,854,405	9,528 (57.29%)	5 (0.03%)
	1–17	148,170 (31.54%)	2.2	8,201	1,216,728,121	97,712 (65.95%)	34 (0.02%)
	18–44	104,400 (22.23%)	3	11,748	1,228,750,528	83,191 (79.68%)	130 (0.12%)
	45–64	111,670 (23.77%)	4	15,626	1,744,778,735	83,997 (75.22%)	404 (0.36%)
	65–84	74,650 (15.89%)	4.9	18,099	1,348,215,082	53,867 (72.16%)	829 (1.11%)
	85+	13,007 (2.77%)	5.3	17,949	233,476,765	9,645 (74.16%)	268 (2.06%)
	Missing	1,211 (0.26%)	2.1	13,197	15,543,940	719 (59.36%)	0 (0.00%)
Region	Northeast	128,928 (27.45%)	3.4	14,979	1,931,237,122	108,523 (84.17%)	429 (0.33%)
	Midwest	98,392 (20.95%)	3.2	9,188	905,320,891	65,535 (66.61%)	330 (0.34%)
	South	171,441 (36.50%)	3.5	11,250	1,928,278,846	114,966 (67.06%)	558 (0.33%)
	West	70,976 (15.11%)	3.3	16,777	1,166,510,716	49,635 (69.93%)	352 (0.50%)

Notes: 2003 dollar values were inflated to 2005 dollars using BLS CPI for Medical Care; ICD-9 code 493; statistics based on 70 or fewer unweighted cases in the nationwide statistics (NIS and KID) are not reliable. These statistics are suppressed and are designated with an asterisk (*).

Source: Weighted national estimates from HCUP Nationwide Inpatient Sample (NIS, 2003), Agency for Healthcare Research and Quality (AHRQ), based on data collected by individual states and provided to AHRQ by the states. Total number of weighted discharges in the United States based on HCUP NIS = 38,220,659 (<http://hcup.ahrq.gov/HCUPnet.asp>).

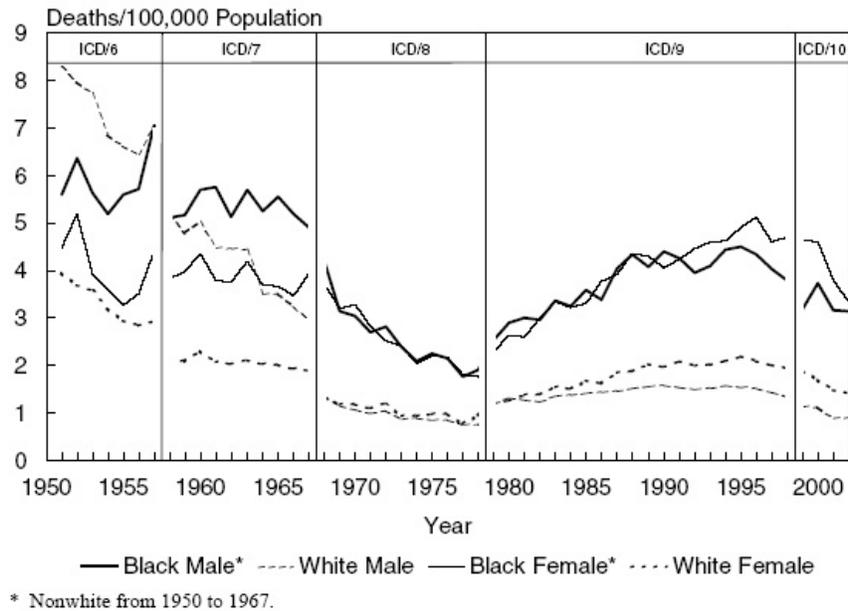


Figure 5-1. Age-adjusted death rates for asthma by race and sex, United States (1951–2002).

Source: NHLBI/NIH (2004). Chartbook on Cardiovascular, Lung, and Blood Diseases (p. 70).

According to a 2000 study (AAAAI, 1996–2005), the direct costs of asthma totaled nearly \$12.5 billion (with hospitalizations the single largest portion of direct cost), and indirect costs (lost earnings due to illness or death) totaled \$9.1 billion. In 2003, the national hospital bill for asthma was \$5.9 billion (see Table 5-4). For the past decade, the number of physician office visits has fluctuated around 10 million per year (see Table 5-3 and Figure 5-2). For adults, asthma is the fourth leading cause of work absenteeism and “presenteeism” (significant lowering of on-the-job productivity) resulting in nearly 15 million missed or “reduced productivity” workdays each year (Mannino et al., 2002). Among children ages 5 to 17, asthma is the leading cause of school absences from a chronic illness. It accounts for an annual loss of more than 14 million school days per year (approximately 8 days for each student with asthma) and more hospitalizations than any other childhood disease (see Figure 5-3). It is estimated that children with asthma spend nearly 8 million days per year restricted to bed (Asthma and Allergy Foundation of America, 2000).

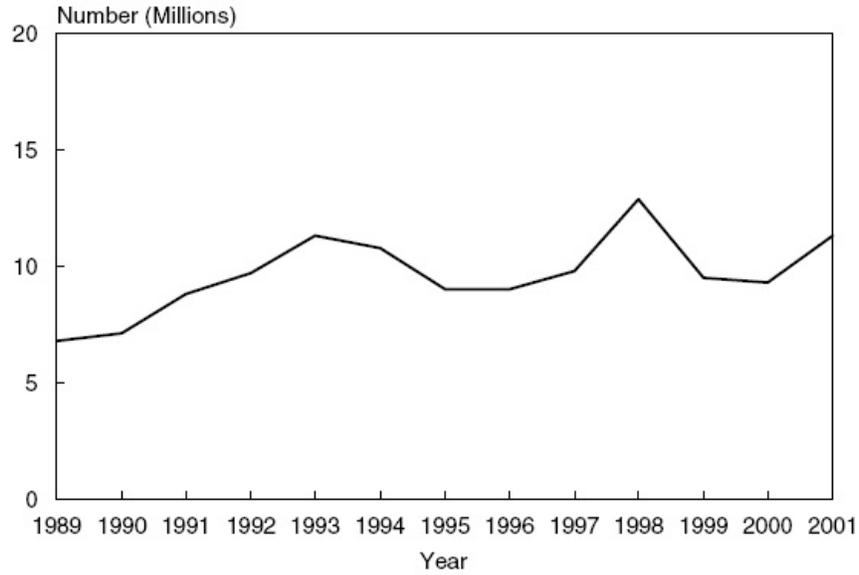


Figure 5-2. Physician office visits for asthma, United States (1989–2001).

Source: NHLBI/NIH (2004). Chartbook on Cardiovascular, Lung, and Blood Diseases (p. 65).

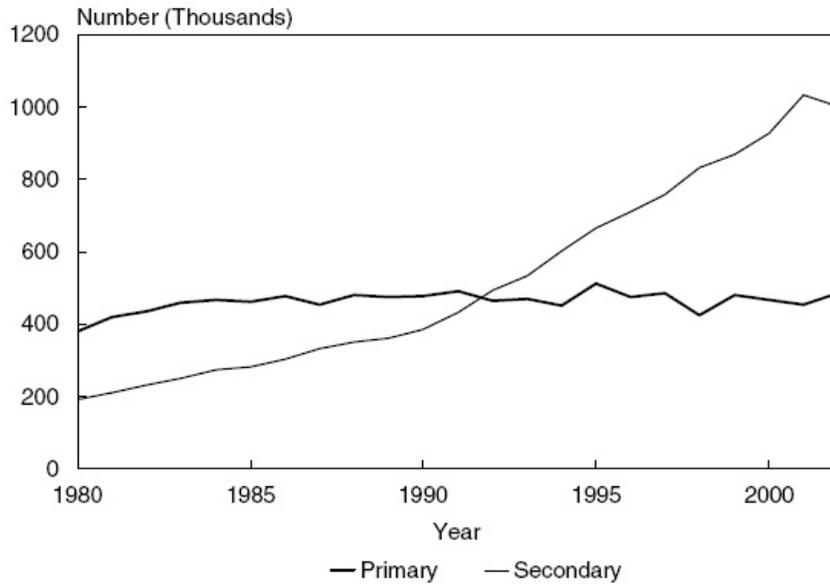


Figure 5-3. Hospitalizations for asthma, United States (1980–2002).

Source: NHLBI/NIH (2004). Chartbook on Cardiovascular, Lung, and Blood Diseases (p. 66).

As noted previously, atopic dermatitis is one of the most common skin diseases, particularly in infants and children. According to the AAAAI (1996–2005), 10–15% of the population is affected during childhood, and there is considerable evidence that the prevalence is increasing. It often precedes other allergic disorders—up to 50% of patients with atopic dermatitis develop asthma. A recent estimate of the direct medical costs associated with atopic dermatitis is \$1.2–\$5.9 billion per annum (Ellis et al., 2002). As in the case of allergic rhinitis, atopic dermatitis seldom results in hospitalization. The total number of hospital discharges with atopic dermatitis listed as the primary diagnosis was 2,582 in 2003, while the aggregate hospital charges totaled \$23 million (see Table 5-5).

Table 5-5. Atopic dermatitis national statistics, 2003—principal diagnosis only

		Total number of discharges	LOS (length of stay), days (mean)	Mean hospital charge (2005\$)	Aggregate charges, (the "national bill") (2005\$)	Admitted from emergency department	In-hospital deaths
All discharges		2,582 (100.00%)	3.2	9,163	23,801,038	1,550 (60.03%)	0 (0.00%)
Age group	<1	212 (8.20%)	3	10,797	2,285,682	109 (51.28%)	0 (0.00%)
	1–17	755 (29.24%)	2.9	8,086	6,134,619	366 (48.48%)	0 (0.00%)
	18–44	465 (17.99%)	2.9	8,379	3,892,126	354 (76.31%)	0 (0.00%)
	45–64	594 (23.01%)	3	8,147	4,840,298	392 (66.06%)	0 (0.00%)
	65–84	474 (18.36%)	3.9	12,009	5,689,869	274 (57.72%)	0 (0.00%)
	85+	67 (2.60%)	4.9	10,877	845,183	44 (65.52%)	0 (0.00%)
	Missing	*	*	*	*	*	*
Region	Northeast	651 (25.20%)	3.2	12,268	7,982,066	508 (78.05%)	0 (0.00%)
	Midwest	551 (21.35%)	3.1	6,864	3,783,047	333 (60.50%)	0 (0.00%)
	South	964 (37.35%)	3.3	8,057	7,769,804	549 (56.95%)	0 (0.00%)
	West	415 (16.09%)	2.8	9,983	4,266,119	159 (38.36%)	0 (0.00%)

Notes: 2003 dollar values were inflated to 2005 dollars using BLS CPI for Medical Care; ICD-9 codes 691.8, 692.9, 373.3 (Ellis et al., 2002); statistics based on 70 or fewer unweighted cases in the nationwide statistics (NIS and KID) are not reliable. These statistics are suppressed and are designated with an asterisk (*).

Source: Weighted national estimates from HCUP Nationwide Inpatient Sample (NIS, 2003), Agency for Healthcare Research and Quality (AHRQ), based on data collected by individual states and provided to AHRQ by the states. Total number of weighted discharges in the United States based on HCUP NIS = 38,220,659 (<http://hcup.ahrq.gov/HCUPnet.asp>).

The impacts these allergic diseases impose on the United States economy and the nonmonetized quality-of-life impacts they impose on the individuals who suffer from them are discussed more fully below. Because cost-of-illness (COI) studies are the primary means by which the direct (medical) and indirect (opportunity) costs of diseases are assessed, an introduction to COI methodology is provided in Subsection 5.1. Recent COI estimates available for asthma, allergic rhinitis, and atopic dermatitis are given in Subsection 5.4.

5.1. COST OF ILLNESS—METHODOLOGY

COI studies are a type of economic study common in the medical literature, particularly in specialist clinical journals. COI studies were pioneered in the late 1950s and early 1960s and have proliferated over the past 30 years. The aim of a COI study is to identify and measure the costs of a particular disease, including the direct (medical) costs, the indirect (opportunity) costs, and the intangible costs (e.g., pain and suffering). A COI study, thus, attempts to estimate the total cost to society of a particular disease and by implication, the amount that would be saved if the disease were abolished. It also identifies the different components of cost and the size of the contribution of each.

The COI study is one of several types of economic evaluation of clinical care, as shown in Figure 5-4. While the COI study focuses on the identification of costs, cost-effectiveness analysis focuses on the relative cost-effectiveness of different treatments, and cost-benefit analysis compares the costs of treatment with the benefits. Economic studies also vary with respect to the perspective (“points of view”) for cost evaluation: society, patient, payor, or provider. Finally, the studies may include different cost components. Thus, even if the studies belong to the same type (e.g.,

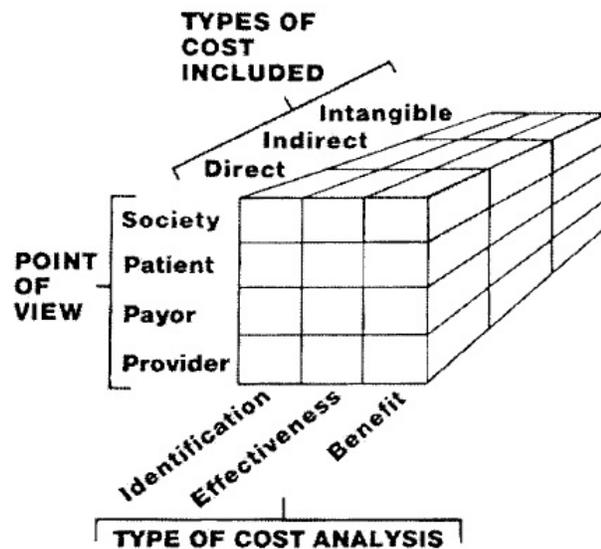


Figure 5-4. Three dimensions of economic evaluation of clinical care.

Source: Bombardier and Eisenberg (1985).

COI), there still may be substantial variability along the other two dimensions (perspective and cost components), which may potentially affect comparability of the estimates. The key distinctions are summarized below.

5.2. COST COMPONENTS

Figure 5-5 summarizes the types of costs that may be subject to evaluation by a given study. COI studies measure the economic burden resulting from disease and illness across a defined population, including both direct and indirect costs. Direct costs are the value of resources used in the treatment, care, and rehabilitation of persons with the condition under study and are, therefore, unavailable to produce other goods and services. Indirect costs represent the value of economic resources lost because of disease-related work disability or premature mortality. In addition, a disease typically involves deterioration in the quality of life of the patient (and his or her family) through its impacts on physical, social, and emotional health—i.e., intangible costs (Kirschstein, 2000).

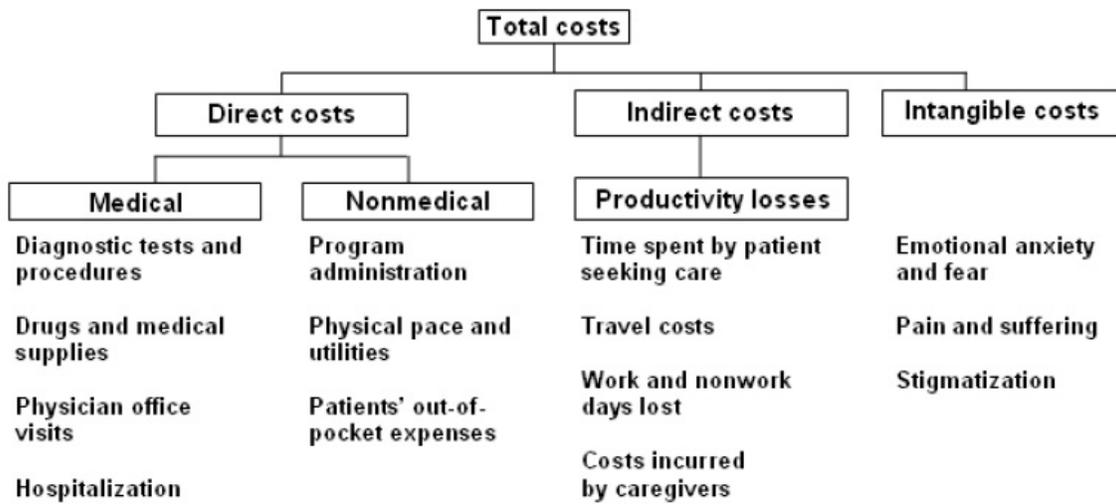


Figure 5-5. Cost inventory diagram.

Source: CDC Economic Evaluation of Public Health Preparedness and Response Efforts (<http://www.cdc.gov/owcd/EET/Cost/Fixed/2.html>).

5.2.1. Direct Medical Costs

Direct medical costs are the costs connected with the use of medical care in the prevention, diagnosis, and treatment of disease and in the continuing care, rehabilitation, or terminal care of patients. Examples include expenditures for hospitalization, outpatient clinical care, nursing home care, and home health care; services of primary physicians and specialists, dentists, and other health practitioners; drugs and drug sundries; and rehabilitation counseling and other rehabilitation costs, such as for prostheses, appliances, eyeglasses, hearing aids, and other devices to overcome impairments resulting from illness or disease. Collectively, these expenditures represent the personal health care component of the United States National Health Expenditures Accounts (Kirschstein, 2000).

5.2.2. Direct Nonmedical Costs

Direct nonmedical costs are the costs borne by patients or other payors that are not included in the National Health Expenditures Accounts. Examples of such costs are expenditures for transportation to hospitals, to physicians' offices, or to other health providers; certain household expenditures (e.g., help for cleaning, laundering, and cooking); special diets and clothing; and relocation and moving expenses (Kirschstein, 2000).

5.2.3. Indirect Costs

Indirect costs are the value of time that patients lose from employment or other productive activity due to mortality or morbidity. These costs also include reduced productivity once the patient returns to work, including unwanted job changes and loss of opportunities for promotion or education, and the value of time lost from work, housekeeping, etc., by family members or friends who transport, visit, and care for patients (Kirschstein, 2000).

5.2.4. Intangible Costs

COI studies rarely attempt to evaluate the intangible costs of disease—the associated pain, suffering, and changes in the quality of life. This issue is of particular importance in the case of chronic diseases (such as those considered here), where there can be a substantial impact on the quality of life over a long period of time (Kirschstein, 2000).

5.2.5. Hidden Costs

There are often, in addition, some “hidden costs” associated with diseases, which are usually neglected by COI studies (Schoenwetter et al., 2004). A disease or condition may contribute to increased costs as a secondary diagnosis, or as a risk factor for other diseases and conditions. For instance, inadequately treated or untreated allergic rhinitis can be associated with a dramatic increase in the cost of caring for comorbid conditions such as asthma, recurrent nasal polyps, sinusitis, and chronic otitis media (Halpern et al., 2004).

5.3. SOURCES OF VARIABILITY IN COST ESTIMATES FROM COI STUDIES

The literature on COI studies documents substantial variation in the methods and data used to estimate the overall costs of illness. Attempts to compare cost data across disease categories should consider the conceptual and methodological issues that may lead to variations in cost estimates. The following are the issues that should be taken into account when considering the COI estimates within and across conditions (see Kirschstein, 2000).

5.3.1. Reference Year

COI estimates are expressed in dollars for a particular reference year. To express all estimates in a common reference year, it is necessary to adjust for changes in the disease burden over time, patterns of treatment and care, and the purchasing power of the dollar for health care services (Kirschstein, 2000).

5.3.2. Cost Components

The comprehensiveness of the estimates of direct and indirect costs differs across studies because of the difficulty and cost required to estimate the nonmedical costs, and the indirect costs related to reduced productivity after returning to the job and the value of services of unpaid care providers. Studies often make a number of specialized assumptions that may drive their results (Kirschstein, 2000).

5.3.3. Discount Rate

In some cases, the present discounted value of the expected stream of lost earnings or medical expenditures incurred over future years is calculated for a base or reference year using a

discount rate intended to reflect people's rate of time preference—i.e., the tradeoff between the value of a dollar received today versus one received next year. The choice of an appropriate discount rate remains controversial and may vary considerably between studies (Kirschstein, 2000).

5.3.4. Definition of Disease

Because the interrelationships among disease categories or causal agents are complex and patients often present more than one disease or condition, it is not always feasible or appropriate to construct mutually exclusive disease categories and associated cost estimates. Cost estimates depend on how narrowly or broadly the disease is defined, whether it includes related conditions beyond its narrowly defined or primary ICD-10 code (International Classification of Diseases version 10), whether the estimate includes identifiable extra costs attributable when the disease is listed as a secondary diagnosis or comorbidity, and whether the estimate includes costs attributable to the disease or condition as an underlying cause or risk factor for other diseases (Kirschstein, 2000).

5.3.5. Prevalence vs. Incidence Approach

COI studies approach cost estimation from either of two perspectives. Most COI studies use the prevalence-based (or annual cost) approach that measures the costs that accrue during a base year due to all existing (or prevalent) cases of disease in that year. In estimating the economic burden resulting from the prevalence of disease, the present discounted value of future losses due to mortality occurring in the base year is calculated. The conventional methodology attributes the future losses to the year in which the death occurs (Kirschstein, 2000).

The incidence-based (or lifetime cost) approach measures the present value of the lifetime costs of the disease for all new (incident) cases with onset of disease during the given base year (Weiss and Sullivan, 1993). Estimation of incidence-based costs requires knowledge of the likely course of a disease and its duration, survival rates, onset, patterns of medical care, and the impact of disease on employment, so it is generally more difficult than estimation of prevalence-based costs. However, the incidence-based approach is sometimes more useful for comparing the effects of alternative interventions to prevent, treat, or manage a particular disease.

5.3.6. Scope and Perspective of Estimation

COI estimates may focus on the total United States resident population, or they may be specific to particular geographic areas or ethnic groups. They may cover all ages, or they may be limited to certain age groups. Similarly, COI studies may estimate costs to the total society, regardless of who bears the costs, or they may estimate the costs to patients, payors, or providers (Kirschstein, 2000).

5.4. COST OF ILLNESS—ESTIMATES

The COI studies discussed below were based on United States data, but varied with respect to scope, perspective, reference year, cost components, and, in some cases, the definition of disease. None of the studies used the incidence approach or applied discount rates to the stream of lost earnings over future years. The majority of COI studies were for asthma, followed by allergic rhinitis and atopic dermatitis.

5.4.1. Allergic Rhinitis

Reed et al. (2004) and Schoenwetter et al. (2004) are two recent comprehensive allergic rhinitis burden-of-disease literature reviews. Two older review papers by Kozma et al. (1996) and Blaiss (2000) discuss the economic and quality-of-life consequences of allergic rhinitis. Finally, O’Connell (2004) and Weiss and Sullivan (2001) discuss allergic rhinitis in the context of atopic diseases, in general.

Table 5-6 summarizes the key features and findings of the original research papers on allergic rhinitis. Direct medical costs and/or indirect costs were estimated by this body of research. However, no attempt was made to monetize the intangible costs of allergic rhinitis. In addition, studies vary in the way they define the condition. Some create estimates for allergic rhinitis only, while others define the disease as “allergic rhinoconjunctivitis” by combining ICD-9 codes for allergic rhinitis and a set of conjunctivitis-related codes (Ray et al., 1999). The direct medical costs of allergic rhinitis range from \$1.7 billion to \$6.2 billion, while indirect costs are estimated to range from \$0.1 billion to \$6.6 billion. Variation in estimates comes largely from different assumptions about prevalence, inclusion of over-the-counter drugs, and partial productivity losses.

Table 5-6. Annual cost of allergic rhinitis/rhinoconjunctivitis estimates, in 2005 \$ by cost category

Study name Period Data sources Methodology	Direct medical costs	Direct nonmedical costs	Hidden costs	Indirect costs		Intangible costs
				Cost of lost school days	Cost of lost work	
Malone et al., 1997 1987 Various U.S. national, NMES, 1987 S, preval. 39 mil	1,741 mil	NA	NA	126 mil		NA
McMenamin, 1994 1985-1990 Various U.S. national S, preval. 22 mil	2,285 mil	NA	NA	1,168 mil		NA
Baraniuk et al., 1996 1990 Various U.S. national S, meta-study	2,393 mil	NA	NA	2,335 mil		NA
Mackowiak, 1997 Various yrs., <i>used 1997 for inflation adjustments</i> Various U.S. national S, preval. 12 mil	6,199 mil	NA	NA	4,137 mil		NA
Law et al., 2003 1996 MEPS S, SR, preval. 12 mil	4,787 mil	NA	NA	NA		NA
Ray et al., 1999 1994 Various U.S. national, NCHS D, S, SR, preval. 27 mil	2,611 mil	NA	5,665 mil	NA		NA
Storms et al., 1997 1993 Population-based survey Incl. OTC, preval. 36 mil	5,331 mil	NA	NA	NA		NA
Kessler et al., 2001 1996-1997 Repr. diary survey of 739 Partial productivity, preval. 13 mil	NA	NA	NA	10,296 mil		NA
Crystal-Peters et al., 2000 1995 Various U.S. national, NHIS/BLS S, preval. 26 mil	NA	NA	NA	6,687 mil		NA
Ross, 1996 1983-1994 Various U.S. national S, preval. 13 mil	NA	NA	NA	5,838 mil		NA

Notes: Bold type indicates a national estimate. Medical costs were inflated to 2005 dollars using BLS CPI for Medical Care; all other costs were inflated to 2005 dollars using BLS CPI. Methodology abbreviations: S = society perspective, SR = self-reported data, OTC = over-the-counter drugs, D = Delphi method used.

There are several methodological issues specific to allergic rhinitis COI studies. First, inadequately treated or untreated allergic rhinitis can be associated with a dramatic increase in the cost of caring for comorbid conditions such as asthma, recurrent nasal polyps, sinusitis, and chronic otitis media (Schoenwetter et al., 2004). These are among the hidden costs of allergic rhinitis. A survey by Halpern et al. (2004) of over 27,398 patients with asthma demonstrated that costs for those with allergic rhinitis and asthma were roughly twice those for patients with asthma alone. Ray et al. (1999) estimate these hidden costs were \$5.7 billion. Blaiss (2000) reports that 58% of patients with asthma, 25% of patients with sinusitis, and 35% of children with otitis media have allergic rhinitis. Second, very few allergic rhinitis COI studies consider the cost of over-the-counter medications. Reed et al. (2004) estimate that 69% of individuals with symptoms of allergic rhinitis used over-the-counter medications in 1993, compared with 45% who used prescription medications. Storms et al. (1997) estimate that the cost of over-the-counter medications was \$90 per patient per year. Thus, excluding the cost of over-the-counter medications will result in a substantial underestimate of the direct medical costs of allergic rhinitis.

Third, the symptoms of allergic rhinitis and sedating side effects of some allergic rhinitis medications are typically not severe enough to cause work absence. However, the symptoms may significantly lower on-the-job productivity (“presenteeism”). Thus, the studies that rely only on estimates of days lost from work are likely to significantly underestimate the indirect costs of allergic rhinitis. In addition, assigning monetary values to decreased work productivity and performance at school is difficult.

Finally, studies by Tripathi and Patterson (2001) and Meltzer (2001) discuss the impact of allergic rhinitis on the quality of life. They point out that poorly controlled symptoms of allergic rhinitis may contribute to loss of sleep, secondary daytime fatigue, learning impairment, decreased cognitive functioning, and decreased long-term productivity. Pharmacological therapies in some cases have considerable adverse side effects, affecting attention, working memory, vigilance, and speed (via sedation mechanism). However, to date no studies have attempted to assign monetary value to the deterioration of quality of life resulting from allergic rhinitis.

5.4.2. Asthma

There is international concern about growing asthma morbidity, and the literature on asthma is very extensive. The review papers that discuss the burden of asthma are Bousquet et al. (2005), Milton et al. (2004), O'Connell (2004), Gergen (2001), Weiss and Sullivan (2001), and Weiss and Sullivan (1993). In addition, there are a number of comprehensive COI studies (Weiss et al., 1992; Weiss et al., 2000; Smith et al., 1997; Farquhar et al., 1998; Birnbaum et al., 2002; Cisternas et al., 2003), including a recent analysis of willingness to pay (WTP) to avoid asthma (Zillich et al., 2002).

Table 5-7 provides a summary of the available asthma COI studies conducted in the United States. As with allergic rhinitis, the studies differ substantially in cost estimates and methods employed; however, importantly, efforts have been made to estimate all known cost components. Direct medical costs range from \$2.7 billion to \$16.9 billion in total (and from \$1,340 to \$3,600 per patient) per annum. Cisternas et al. (2003) estimated \$579 per patient in direct nonmedical costs. Hidden costs were estimated to be \$2,450 per patient in extra direct medical costs for asthma comorbidities and \$373 per patient in work loss costs due to exacerbating effects of asthma on related conditions (Birnbaum et al., 2002).

Total indirect costs are not always comparable due to differences in components included. Estimates that include loss of life are substantially higher (\$2.6 billion to \$6.1 billion as compared to \$0.9 billion). In addition to these estimates, a recent comprehensive study of productivity loss by Ward et al. (2002) reports that 25.2% of asthma patients in their sample were unable to work, 17.5% were limited in kind or amount of work, and 47.2% attributed the limitation in their ability to work to asthma.

Weiss and Sullivan (2001) noted that (1) asthma imposes a considerable financial burden on the family, which may adversely affect access to care by poorer individuals; and (2) emergency department visits and hospitalizations are the key components of asthma care, with estimated costs per family of \$2,784–\$4,057 per annum. Hospitalization and medication represent two thirds to three quarters of total direct asthma-related costs (Gergen, 2001). Stanford et al. (1999) conclude that nursing accounts for the largest portion of hospital costs (43.6%), followed by respiratory therapy (13.6%), and medications (10.4%). Based on international comparisons, the percent of direct costs associated with hospitalization appears to be inversely correlated with the percent associated with medications (Gergen, 2001). This

Table 5-7. Annual cost of asthma estimates, in 2005 \$ by cost category

Study name Period Data sources Methodology	Direct medical costs	Direct nonmedical costs	Hidden costs	Indirect costs			Intangible costs
				Cost of lost school days	Cost of lost work	Loss of life	
Vance and Taylor, 1971 1967–1969 3-year panel of 21 families with active asthmatics F	2,903/ family	NA	NA	NA			NA
US NHLI, 1972 1967 Various U.S. National data sources S	2,784 mil	NA	NA	1,591 mil			NA
Marion et al., 1985 1977–1980 <i>used 1980 for inflation adjustments</i> 1-year panel of 30 families with asthmatic child F	4,057/ family	NA	NA	348/ family			NA
Weiss et al., 1992 1985 Various U.S. National data sources S, CHG, SR	7,633 mil	NA	NA	2,624 mil			NA
				911 mil	866 mil	847 mil	
Smith et al., 1997 1987 NMES S, SR	7,883 mil	NA	NA	890 mil^a			NA
				257 mil	555 mil	NA	
Farquhar et al., 1998 1996 1987 NMES, S	16,995 mil	NA	NA	2,489 mil			NA
Weiss et al., 2000 1994 Various U.S. National data sources S, CHG, SR	9,357 mil	NA	NA	6,116 mil			NA
				1,261 mil	2,725 mil	2,130 mil	
Birnbaum et al., 2002 1996–1998 <i>used 1998 for inflation adjustments</i> Claims data for Fortune 100 national company E, case-control	1,340/ patient	NA	2,450 ^b / 373 ^c / patient	NA	138/ patient	NA	NA
Zillich et al., 2002 2002 (<i>used 2002 for inflation adjustments</i>) Survey 100 asthmatics from community pharmacies in KY / P, WTP	NA	NA	NA	NA			2,102 ^d / 1,599 ^e / patient
Cisternas et al., 2003 1998–1999 MEPS, NCS, panel of 401 adults from a sample of CA providers S	3,600/ patient	579/ patient	NA	NA	2,074/ patient	NA	NA

^aComponents may not add up to the total because other categories of indirect costs included bed days for children under 4.

^bExtra direct medical costs for other asthma-related conditions.

^cExtra loss of work costs for other asthma-related conditions.

^dObjective willingness to pay; ^e = subjective willingness to pay.

Notes: Bold type indicates a national estimate. Medical costs were inflated to 2005 dollars using BLS CPI for Medical Care; all other costs were inflated to 2005 dollars using BLS CPI. Methodology abbreviations: F = family perspective, S = society perspective, E = employer perspective, P = patient perspective, CHG = includes hospital charges and not costs, WTP = willingness to pay, SR = self-reported data.

relationship may reflect the well-known fact that adequately managed asthma can reduce hospitalizations. The cost of asthma can be substantially nonuniform across asthmatics. Smith et al. (1997) noted that less than 20% of the individuals with asthma in their sample accounted for more than 80% of the total direct costs.

Finally, Zillich et al. (2002) estimated WTP to avoid asthma, the only measure that would include the intangible costs of the illness. Their survey of one hundred patients with asthma (recruited from Kentucky pharmacies) suggested that WTP was significantly related to both objective disease severity (as defined by a physician) and disease severity subjectively assessed by the patient. For objective disease severity, the mean monthly WTP was \$97 for mild asthma, \$142 for moderate asthma, and \$359 for severe asthma. For subjective disease severity, the mean monthly WTP was \$52 for mild asthma, \$180 for moderate asthma, and \$262 for severe asthma. A weighted annual average is \$2,102 for objective WTP and \$1,599 for subjective WTP per patient.

5.4.3. Atopic Dermatitis

A recent review paper by Carroll et al. (2005) on the burden of atopic dermatitis on patients, family, and society indicates that COI estimates for atopic dermatitis are very limited in the United States. This is despite the fact that atopic dermatitis is widespread and is generally considered to be associated with substantial deteriorations in quality of life for patients and their families. In addition, O'Connell (2004) notes that atopic dermatitis can have a large social/emotional and financial effect on the family and often predates the development of allergic rhinitis and asthma.

Table 5-8 summarizes the available United States evidence. Lapidus et al. (1993) studied emergency room visits and ambulatory care billing records of an urban hospital in Philadelphia and extrapolated the direct costs to the United States to be \$665 million annually. However, this study, published in 1993, was thought to underestimate the true cost of atopic dermatitis because it included only ER and physician visits (Carroll et al., 2005).

In a systematic review of third party claims data, Ellis et al. (2002) estimated the direct cost of atopic dermatitis in the United States to be \$1.2–\$5.2 billion. This analysis used claims from a managed care payor and state Medicaid program, with atopic dermatitis diagnoses based on International Classification of Diseases (ICD-9-CM) codes. Claims were reviewed by a

Table 5-8. Annual cost of atopic dermatitis estimates, in 2005 \$ by cost category.

Study name Period Data sources Methodology	Direct medical costs	Direct nonmedical costs	Hidden costs	Indirect costs		Intangible costs
				Cost of lost school days	Cost of lost work	
Lapidus et al., 1993 1991 Philadelphia Children Hospital S, national estimate	665 mil^a	NA	NA	NA		NA
Ellis et al., 2002 1997 Claims data (private provider and a state Medicaid program) PAY, D, case control	1,239 mil- 5,234 mil or 1,460/ person ^b	NA	NA	NA		NA
Fivenson et al., 2002 1997 Survey of 248 individuals in a managed care population P, OTC	427/person	NA	NA	4111/person		NA

^aLikely to underestimate direct medical costs because includes only ER and physician’s office visits.

^bEstimate for privately insured individuals was \$799/person.

Notes: Bold type indicates a national estimate. Medical costs were inflated to 2005 dollars using BLS CPI for Medical Care; all other costs were inflated to 2005 dollars using BLS CPI. Methodology abbreviations: S = society perspective, PAY = payor perspective, P = patient perspective, OTC = over-the-counter drugs, D = Delphi method.

panel, and comorbidities were classified as most likely related to atopic dermatitis and possibly related to atopic dermatitis (using the Delphi method to create consensus, as explained in [Powell, 2003]). The cost quoted included all atopic dermatitis claims for visits, prescription drugs, and “likely” atopic dermatitis-related comorbidities. The estimate, however, did not include the costs of over-the-counter medications or any indirect costs of lifestyle changes.

Fivenson et al. (2002) estimated the direct and indirect costs of atopic dermatitis at \$838 per patient annually, using a patient survey to determine the indirect costs (including time lost from work) and managed care claims data to assess the direct costs. The direct medical costs (not including over-the-counter medications) were found to be only 27% of the total, suggesting the significant underestimation that occurs if only direct costs are used to estimate the economic burden of atopic dermatitis. Additionally, as discussed in an editorial by Ellis et al. (2003), there

may have been an unrepresentatively small number of severely affected patients in Fivenson's study sample, which would lead to lower cost estimates (Carroll et al., 2005).

As noted above, atopic dermatitis is often associated with significant morbidity. Pruritus (severe itching, often of undamaged skin) caused by atopic dermatitis can affect both sleep and mood, and affected individuals often must modify several aspects of their lives because of treatment regimens and associated lifestyle changes. Individuals with atopic dermatitis are also at risk for psychosocial difficulties that may have long-lasting consequences, potentially affecting career choices and personal relationships. Patients are thus affected both by the condition itself and by the stigma associated with its visibility. A number of studies have shown that people with atopic dermatitis tend to report lower health-related quality of life and greater psychological distress than the general population (Carroll et al., 2005). In addition, the effects of atopic dermatitis on the entire family can be extensive. Unfortunately, monetary assessments of these intangible costs in the United States are yet to come.

6. FUTURE RESEARCH

Further progress must be made in documenting and understanding aeroallergen response to climate, the role of aeroallergens in disease development, and the willingness to pay to avoid—the intangible costs of these allergic diseases.

A review of the literature indicates that there are limited data on aeroallergen trends in the United States. Integrated long-term data series on all aeroallergens is necessary to clearly document future changes in aeroallergen production and distribution, as well as allergen content. Additional research on the response of mold and indoor allergens to climate change would be of particular value. In addition, further experimental and field studies are needed to examine how allergen content and distribution of aeroallergens may be altered in response to climate change. Such studies could address a number of key issues, including (1) the combined effects of CO₂ and temperature, as well as interactions between these and other important variables, such as water and nutrient availability, disturbance, and competition (Beggs, 2004); (2) within-species genetic variation in response to changing CO₂ concentration availability and temperature (Beggs, 2004); and (3) effects of urban warming or land use changes, which may alter observed impacts of climate change (Beggs, 2004).

There is a need for better understanding of the role of aeroallergens in disease development, especially asthma, specifically, what the relative contribution of different aeroallergens is to the development of asthma (Selgrade et al., 2006). There is a need to know what levels of allergen exposure constitute a risk for development of asthma (Selgrade et al., 2006). There is also a need for standardized approaches for measuring exposures and outcomes in epidemiologic studies (Selgrade et al., 2006). Finally, the possible synergistic effects of aeroallergens and air pollutants on the development of allergic diseases could be an important area for future research. For example, changes in the timing of pollen seasons could result in some overlap between the peak pollen period and the ozone season.

Based on a review of the COI literature on allergic rhinitis, asthma, and atopic dermatitis, it is clear that an important research gap is the current lack of assessment of—and, in particular, estimation of, willingness to pay to avoid the intangible costs of these diseases. In addition, better methodologies are needed to address productivity losses, aeroallergen avoidance, and over-the-counter medication use. Finally, as noted in Section 5, a disease or condition may

contribute to increased costs as a secondary diagnosis, or as a risk factor for other diseases and conditions. These hidden costs of comorbidity need to be properly estimated and, if possible, included in future COI studies.

7. SUMMARY AND CONCLUSIONS

This report reviewed the available literature on (1) aeroallergens and associated allergic diseases prevalent in the United States; (2) the potential impacts of climate change on these aeroallergens and, by inference, on the allergic diseases associated with them; and (3) the economic and quality-of-life impacts of these diseases. Although some of the relevant research cited was carried out in other countries, this report focuses on the United States.

Aeroallergens are distributed throughout the United States, but some are concentrated in particular geographic regions. Three allergic diseases have been associated with aeroallergens in the United States: asthma, allergic rhinitis (hay fever), and atopic dermatitis (eczema). Although all aeroallergens have been linked to each of these three allergic diseases, the strongest associations appear to be between pollen (tree, grass, or weed) and allergic rhinitis (hay fever), and between house dust mites or mold and asthma.

Limited data suggest aeroallergen levels in the United States have remained relatively constant (though the period of record may be too short to assess trends). While significant increases in the prevalence of allergic diseases have been observed, the factors contributing to this increase remain unclear. At the same time, experts have hypothesized that an increase in the distribution and concentration of aeroallergens could further increase the economic and quality-of-life burdens imposed by these diseases in the United States.

The literature does not provide definitive data or conclusions on how climate change might impact aeroallergens and subsequently the severity and prevalence of allergic diseases in the United States. There is also an inherent uncertainty as to how the climate will change, especially at a regional level. In addition, the etiology of allergic diseases, especially asthma, is complex and has a gene environment interaction that is poorly understood. Finally, there are numerous other factors that affect aeroallergen levels and the prevalence of associated allergic diseases, such as changes in land use, air pollution, adaptive responses, and modifying factors; many of which are difficult to assess.

Nevertheless, some tentative inferences can be drawn about the potential impact of climate change on aeroallergens and the associated allergic diseases by making reasonable inferences about the links between (1) climate change and the characteristics of aeroallergens and (2) those aeroallergen characteristics and the associated allergic diseases. Global climate

models developed for the NAST suggest that many areas of the United States will become warmer and wetter. In addition, research has shown that pre-season temperature and precipitation have been consistently important projectors of pollen and mold production. Moreover, atmospheric carbon dioxide concentration has increased and will continue to increase, and this alone will have impacts on aeroallergens, regardless of changes in precipitation and temperature. Overall, experimental and observational data, as well as models, indicate the following likely changes in aeroallergen production, distribution, dispersal, and allergen content as a result of climate change in the United States:

- Pollen production is likely to increase in many parts of the United States, with the possible exception of the Southeast
- Phenologic advance (i.e., earlier start of pollen season) is likely to occur for numerous species of plants, especially trees (Root et al., 2003)
- There will likely be changes in the distribution of pollen-producing species, including the possibility of extinction in some cases and expansion in others (Joyce et al., 2001)
- Intercontinental dispersal (e.g., of pollen) is possible, facilitating the introduction of new aeroallergens into the United States (Husar et al., 2001)
- Increases in allergen content of some aeroallergens are possible (Beggs, 2004; Beggs and Bambrick, 2005)

Aeroallergen (e.g., pollen) exposure in sensitized individuals is associated with allergic rhinitis and less clearly with asthma and atopic dermatitis. Furthermore, some studies have demonstrated links between weather, aeroallergen production, and subsequent increased illness. Therefore, we can infer that changes in the timing, severity, and possibly the prevalence of allergic rhinitis (hay fever) are likely, given the clear association between allergen exposure and response in sensitized individuals. While recent research points to a link between aeroallergens and asthma, the complex etiology of this illness and the unclear link between indoor aeroallergens and climate change lead to greater uncertainty about how asthma severity or prevalence might change in response to climate change and corresponding impacts on aeroallergens.

Because the economic and quality-of-life impacts of these allergic diseases are substantial, the corresponding economic and quality-of-life impacts of increases in the prevalence of these diseases could similarly be significant. It has been reported that 54.6% of people in the United States currently test positive to one or more allergens. Consequently, allergies are the sixth most costly chronic disease category in the United States, costing the health care system approximately \$21 billion annually (in 2005 dollars). Although the allergic diseases discussed in this report—allergic rhinitis, asthma, and atopic dermatitis—are not the only allergic diseases in the United States, they are among the most important ones, and the costs associated with them account for a substantial component of the total costs of allergies in the United States.

Allergic rhinitis affects approximately 40 million people each year in the United States, 40% of whom are children. Estimated total direct costs of treatment are \$6.2 billion per year (in 2005 dollars). Indirect costs include 3.8 million missed days of school and work per year.

Asthma is estimated to affect approximately 15 million Americans, and 30% of all patients are children. Asthma can be life-threatening—there were 1,669 deaths due to asthma in 2003. According to a 2000 study, direct costs totaled nearly \$12.5 billion (in 2005 dollars) and indirect costs (lost earnings due to illness or death) totaled \$9.1 billion (in 2005 dollars). For adults, asthma is the fourth leading cause of work losses, resulting in nearly 15 million missed or “reduced productivity” workdays each year. Among children, asthma is the leading cause of school absences from a chronic illness, resulting in an annual loss of more than 14 million school days per year.

Atopic dermatitis is one of the most common skin diseases, particularly in infants and children—10 to 15% of the population is affected during childhood, and there is considerable evidence that the prevalence is increasing. The direct medical costs associated with atopic dermatitis are estimated to be \$1.2–\$5.9 billion (in 2005 dollars) per annum.

The cost of illness studies for allergic rhinitis, asthma, and atopic dermatitis that contributed to this review were all based on United States data, but varied with respect to scope, perspective, reference year, cost components, and, in some cases, the definition of disease. None of the studies used the incidence approach or applied discount rates to the stream of lost earnings over future years.

REFERENCES

- Adinoff, AD; Tellez, P; Clark, RA. (1988) Atopic dermatitis and aeroallergen contact sensitivity. *J Allergy Clin Immunol* 81(4):736–742.
- Ahlholm, JU; Helander, ML; Savolainen, J. (1998) Genetic and environmental factors affecting the allergenicity of birch (*Betula pubescens* ssp. *czerepanovii* [Orl.] Hamet-ahti) pollen. *Clin Exp Allergy* 28(11):1384–1388.
- AAAAI (American Academy of Allergy, Asthma & Immunology). (1996–2006) Allergy statistics. [Cited 2006 April 2006]. Available from http://www.aaaai.org/media/resources/media_kit/allergy_statistics.stm.
- AAAAI (American Academy of Allergy, Asthma & Immunology). (2002) Common Outdoor Allergens. [Cited 2006 April 11]. Available from: http://www.aaaai.org/nab/index.cfm?p=common_outdoor_allergens.
- AAAAI (American Academy of Allergy, Asthma & Immunology). (1996–2005) The allergy report: science based findings on the diagnosis & treatment of allergic disorders. [Cited. Available from <http://www.theallergyreport.com/reportindex.html>.
- American College of Allergy. (2006) Five most troublesome allergens. [Cited 2006 April 12]. Available from <http://www.acaai.org/public/facts/5allergens.htm>.
- Andersson, M; et al. (2003) Natural exposure to *Alternaria* spores induces allergic rhinitis symptoms in sensitized children. *Pediatric Allergy and Immunology* 14(2):100–105.
- Arbes, S. J., et al. Prevalences of positive skin test responses to 10 common allergens in the US population: results from the third National Health and Nutrition Examination Survey. *J Allergy Clin Immunol*, 2005. 116(2): p. 377–83.
- Asero, R., 2002: Birch and ragweed pollinosis north of Milan: a model to investigate the effects of exposure to "new" airborne allergens. *Allergy*, 57, 1063–6
- Asthma and Allergy Foundation of America, A. 2000. The Costs of Asthma. [Cited. Available from: <http://www.aafa.org/display.cfm?id=6&sub=63>
- Baraniuk, J., E. Meltzer, and S. Spector. Impact of allergic rhinitis and related airway disorders. *J Respir Dis*, 1996. 17(Suppl.): p. 511–23.
- Beggs, P.J.. Pollen and pollen antigen as triggers of asthma: what to measure. *Atmospheric Environment*. 1998. 32(10): 1777–1783.
- Beggs, P. J. Impacts of climate change on aeroallergens: past and future. *Clin Exp Allergy*, 2004. 34(10): p. 1507–13.
- Beggs, P. J. and H. J. Bambrick. Is the global rise of asthma an early impact of anthropogenic climate change? *Environ Health Perspect*, 2005. 113(8): p. 915–9.
- Bennett, J. W. The Molds of Katrina. *New York Academy of Sciences*, 2006. January/February 2006: p. 6–9.
- Bernard, S. M., et al. The potential impacts of climate variability and change on air pollution-related health effects in the United States. *Environ Health Perspect*, 2001. 109 Suppl 2: p. 199–209.
- Birnbaum, H. G., et al. Direct and indirect costs of asthma to an employer. *J Allergy Clin Immunol*, 2002. 109(2): p. 264–70.

- Blaiss, M. S. Cognitive, social, and economic costs of allergic rhinitis. *Allergy Asthma Proc*, 2000. 21(1): p. 7–13.
- Bombardier, C. and J. Eisenberg. Looking into the crystal ball: can we estimate the lifetime cost of rheumatoid arthritis? *J Rheumatol*, 1985. 12(2): p. 201–4.
- Bousquet, J., et al. The public health implications of asthma. *Bull World Health Organ*, 2005. 83(7): p. 548–54.
- Breton MC, Garneau M, Fortier I, Guay F, Louis J. 2006. Relationship between climate, pollen concentrations of Ambrosia and medical consultations for allergic rhinitis in Montreal, 1994–2002. *Sci Total Environ*, 370(1): 39–50.
- Burge, H. A. An update on pollen and fungal spore aerobiology. *J Allergy Clin Immunol*, 2002. 110(4): p. 544–52.
- Burr, M. L. Grass pollen: trends and projections. *Clin Exp Allergy*, 1999. 29(6): p. 735–8.
- Bush, R. K. and J. J. Prochnau. Alternaria-induced asthma. *J Allergy Clin Immunol*, 2004. 113(2): p. 227–34.
- Carroll, C. L., et al. The burden of atopic dermatitis: impact on the patient, family, and society. *Pediatr Dermatol*, 2005. 22(3): p. 192–9.
- Cecchi, L., M. Morabito, M. Paola Domeneghetti, A. Crisci, M. Onorari and S. Orlandini, 2006: Long distance transport of ragweed pollen as a potential cause of allergy in central Italy. *Ann. Allergy. Asthma. Immunol.*, 96, 86–91
- Cisternas, M. G., et al. A comprehensive study of the direct and indirect costs of adult asthma. *J Allergy Clin Immunol*, 2003. 111(6): p. 1212–8.
- Clark RAF and AD Adinoff. *Aeroallergen contact can exacerbate atopic dermatitis patch tests as diagnostic tests*. *Journal of American Academy of Dermatology*. 1989. 21(2) 863–869
- Clot, B. Trends in airborne pollen: An overview of 21 years of data in Neuchâtel (Switzerland). *Aerobiologia*, 2003. 19(3–4): p. 227–234.
- Corden, J. M. and W. M. Millington. The long-term trends and seasonal variation of the aeroallergen Alternaria in Derby, UK. *Aerobiologia*, 2001. 17: p. 127–136.
- Corden, J.M., W.M. Millington and J. Mullins, 2003: Long-term trends and regional variation in the aeroallergens in Cardiff and Derby UK. Are differences in climate and cereal production having an effect? *Aerobiologia*, 19, 191
- Comtois, P and L Gagnon. *Pollen concentration and frequency of pollinosis symptoms*. *French Review of Allergies* 1988. 28(4): 279–286
- Crystal-Peters, J., et al. The cost of productivity losses associated with allergic rhinitis. *Am J Manag Care*, 2000. 6(3): p. 373–8.
- Custovic, A., et al. Controlling indoor allergens. *Annals of Allergy, Asthma and Immunology*, 2002. 88(5): p. 432 – 442.
- Dales, R. E., et al. The role of fungal spores in thunderstorm asthma. *Chest*, 2003. 123(3): p. 745–50.
- D’Amato G, Liccardi G, D’Amato M, Cazzola M. Outdoor air pollution, climatic changes and allergic bronchial asthma. *Eur Respir J* 2002; 20:763–76.
- D’Amato G and Cecchi L. 2008. Effects of climate change on environmental factors in respiratory allergic diseases. *Clinical and Experimental Allergy*, 1–11. doi: 10.1111/j.1365-2222.2008.03033.x

- Davis, M. B. and R. G. Shaw. Range Shifts and Adaptive Responses to Quaternary Climate Change. *Science*, 2001. 292: p. 673–679.
- Dvorin, D. J., et al. A comparative, volumetric survey of airborne pollen in Philadelphia, Pennsylvania (1991–1997) and Cherry Hill, New Jersey (1995–1997). *Ann Allergy Asthma Immunol*, 2001. 87(5): p. 394–404.
- Ellis, C. N., et al. Cost of atopic dermatitis and eczema in the United States. *J Am Acad Dermatol*, 2002. 46(3): p. 361–70.
- Ellis, C. N., et al. Validation of expert opinion in identifying comorbidities associated with atopic dermatitis/eczema. *Pharmacoeconomics*, 2003. 21(12): p. 875–83.
- Emberlin, J. The effects of patterns in climate and pollen abundance on allergy. *Allergy*, 1994. 49(18 Suppl): p. 15–20.
- Emberlin, J., et al. Responses in the start of *Betula* (birch) pollen seasons to recent changes in spring temperatures across Europe. *Int J Biometeorol*, 2002. 46(4): p. 159–70.
- Emberlin, J., et al. Regional variations in grass pollen seasons in the UK, long-term trends and forecast models. *Clin Exp Allergy*, 1999. 29(3): p. 347–56.
- Epton, M. J., et al. Climate and aeroallergen levels in asthma: a 12 month prospective study. *Thorax*, 1997. 52(6): p. 528–34.
- Erbas B, Chang JH, Charmage S, Ong EK, Hyndman R, Newbiggin E, Abramson M. 2007. Do levels of airborne grass pollen influence asthma hospital admissions? *Clin Exp Allergy*, 37(11): 1641–7.
- Farquhar et al. Cost estimates for environmentally related asthma, in *Research in Human Capital and Development* (Vol. 12), A. Sorkin and I. Farquhar, Editors. 1998. p. 35–46.
- Fivenson, D., et al. The Effect of Atopic Dermatitis on Total Burden of Illness and Quality of Life on Adults and Children in a Large Managed Care Organization. *J Managed Care Pharm*, 2002. 8(5): p. 333–42.
- Frenguelli, G. Interactions between climatic changes and allergic plants. *Monaldi Arch Chest Dis*, 2002. 57(2): p. 141–3.
- Freye, K., Litwin, C.M. Variations of Pollen and Mold Concentrations in 1998 during the Strong El Niño Event of 1997–1998 and Their Impact on Clinical Exacerbations of Allergic Rhinitis, Asthma, and Sinusitis. *Allergy and Asthma Proceedings*, 2001. 22(4): p. 239–247(9).
- Galan, C., et al. Heat requirement for the onset of the *Olea europaea* L. pollen season in several sites in Andalusia and the effect of the expected future climate change. *Int J Biometeorol*, 2005. 49(3): p. 184–8.
- Galant, S., et al. Prevalence of Sensitization to Aeroallergens in California Patients with Respiratory Allergy. *Annals of Allergy, Asthma and Immunology*, 1998. 81(3): p. 203–210.
- García-Mozo H, Galan C, Jato V, Belmonte J, de la Guardia C, Fernandez D, Gutierrez M, Aira M, Roure J, Ruiz L, Trigo M, Dominguez-Vilches E. 2006. *Quercus* pollen season dynamics in the Iberian Peninsula: response to meteorological parameters and possible consequences of climate change. *Ann Agric Environ Med.*, 13(2): 209–24.
- Gergen, P. J. Understanding the economic burden of asthma. *J Allergy Clin Immunol*, 2001. 107(5 Suppl): p. S445–8.
- Gilmour, M. I., et al. How exposure to environmental tobacco smoke, outdoor air pollutants, and increased pollen burdens influences the incidence of asthma. *Environ Health Perspect*, 2006. 114(4): p. 627–33.

- Glassheim, J. W., et al. Analysis of meteorologic variables and seasonal aeroallergen pollen counts in Denver, Colorado. *Ann Allergy Asthma Immunol*, 1995. 75(2): p. 149–56.
- Gonzalez Minero, F. J., et al. Airborne grass (Poaceae) pollen in southern Spain. Results of a 10-year study (1987–96). *Allergy*, 1998. 53(3): p. 266–74.
- Green, B. J., et al. Atmospheric Poaceae pollen frequencies and associations with meteorological parameters in Brisbane, Australia: a 5-year record, 1994-1999. *Int J Biometeorol*, 2004. 48(4): p. 172–8.
- Griffin DW, Garrison VH, Herman JR, & Shinn EA. 2001. African desert dust in the Caribbean atmosphere: microbiology and public health. *Aerobiologia*, 17, 203–213.
- Griffin DW, Westphal DL, Gray MA. 2006. Airborne microorganisms in the African desert dust corridor over the mid-Atlantic ridge, Ocean Drilling Program. *Aerobiologia* 22: 211–226.
- Halonen, M., et al. *Alternaria* as a major allergen for asthma in children raised in a desert environment. *Am J Respir Crit Care Med*, 1997. 155(4): p. 1356–61.
- Halpern, M. T., et al. Allergic rhinitis: a potential cause of increased asthma medication use, costs, and morbidity. *J Asthma*, 2004. 41(1): p. 117–26.
- Hamilton, R. G. Assessment of indoor allergen exposure. *Curr Allergy Asthma Rep*, 2005. 5(5): p. 394–401.
- Hamilton, R. G. and P. A. Eggleston. Environmental allergen analyses. *Methods*, 1997. 13(1): p. 53–60.
- Héguy L, Garneau M, Goldberg MS, Raphoz M, Guay F, Valois MF. 2008. Associations between grass and weed pollen and emergency department visits for asthma among children in Montreal. *Environ Res*. 106(2): 203–11.
- Henderson, C. E., et al. Projecting asthma severity from allergic sensitivity to cockroaches in pregnant inner city women. *J Reprod Med*, 2000. 45(4): p. 341–4.
- Hollins, P. D., et al. Relationships between airborne fungal spore concentration of *Cladosporium* and the summer climate at two sites in Britain. *Int J Biometeorol*, 2004. 48(3): p. 137–41.
- Horner, WE, Helbing, A, Salvaggio, JE, and Lehrer SB. 1995. Fungal Allergens. *Clinical Microbiology Reviews* 8(2): 161–179.
- Husar, R. B., et al. Asian dust events of April 1998. *Journal of Geophysical Research*, 2001. 106(D12): p. 18,317–18,330.
- IPCC, 2007: *Climate Change 2007: The Physical Science Basis. Contribution of Working Group I to the Fourth Assessment Report of the Intergovernmental Panel on Climate Change* [Solomon, S., D. Qin, M. Manning, Z. Chen, M. Marquis, K.B. Averyt, M. Tignor and H.L. Miller (eds.)]. Cambridge University Press, Cambridge, United Kingdom and New York, NY, USA, 996 pp..
- Jablonski LM, X Wang and PS Curtis. Plant reproduction under elevated CO₂ conditions: a meta-analysis of reports on 79 crop and wild species. 2002. *New Phytologist*. 156: 9–26.
- Joint Task Force on Practice Parameters, American Academy of Allergy, Asthma and Immunology. 2003. *The Major Clinically Relevant Aeroallergens of North America*. Updated: Last Update January. [Cited Access 2003 2006]. Available from: <http://www.jcaai.org/PP/images/1TT2.gif>
- Joyce, L., et al. *Potential Consequences of Climate Variability and Change for the Forests of the United States, in Climate Change Impacts on the United States: The Potential Consequences of Climate Variability and Change*, United States Global Change Research Program, Editor. 2001, Cambridge University Press: Cambridge.

- Katial, R. K., et al. Atmospheric mold spore counts in relation to meteorological parameters. *Int J Biometeorol*, 1997. 41(1): p. 17–22.
- Kemp, AS. *Relationship between the time of birth and the development of immediate hypersensitivity to grass pollen antigens*. *Medical Journal of Australia*. 1979. 1(7) 263–264
- Kessler, R., et al. Pollen and mold exposure impairs the work performance of employees with allergic rhinitis. *Ann Allergy Asthma Immunol.*, 2001. 87(4): p. 289–95.
- Kirschstein, R. Disease Specific Estimates of Direct and Indirect Costs of Illness and NIH Support. Fiscal Year 2000 Update, N. US DHHS, Editor. 2000.
- Knapp PA. and Soulé P T. 1998. Recent *Juniperus occidentalis* (western juniper) expansion on a protected site in central Oregon. *Global change Biology*, 4: 347–357.
- Knowlton K, Rotkin-Ellman M, Solomon G (2007) Sneezing and Wheezing: How Global Warming Could Increase Ragweed Allergies, Air Pollution, and Asthma. Natural Resources Defense Council. <http://www.nrdc.org/globalWarming/sneezing/sneezing.pdf>
- Kosisky, S. E. and G. B. Carpenter. Predominant tree aeroallergens of the Washington, DC area: a six year survey (1989–1994). *Ann Allergy Asthma Immunol*, 1997. 78(4): p. 381–92.
- Kozma, C. M., M. K. Sadik, and M. L. Watrous. Economic Outcomes for the Treatment of Allergic Rhinitis. *PharmacoEconomics*, 1996. 10(1): p. 4–13.
- Lapidus, C., D. Schwarz, and P. Honig. Atopic dermatitis in children: who cares? Who pays? *J Am Acad Dermatol*, 1993. 28(5 Pt 1): p. 699–703.
- Lapidus, C. S. Role of social factors in atopic dermatitis: the US perspective. *J Am Acad Dermatol*, 2001. 45(1 Suppl): p. S41–3.
- Law, A. W., et al. Direct costs of allergic rhinitis in the United States: estimates from the 1996 Medical Expenditure Panel Survey. *J Allergy Clin Immunol*, 2003. 111(2): p. 296–300.
- Lawson, J. A. and A. Senthilselvan. Asthma epidemiology: has the crisis passed? *Curr Opin Pulm Med*, 2005. 11(1): p. 79–84.
- Levetin, E. Effect of Climate Change on Airborne Pollen. in *American Academy of Allergy, Asthma and Immunology 57th Annual Meeting*. 2001. New Orleans, LA: The Journal of Allergy and Clinical Immunology.
- Levetin, E. 2006. Dr. Estelle Levetin's HomePage. [Cited 2006 May 12]. Available from: <http://pollen.utulsa.edu/>
- Levetin, E. and P. K. Van de Water. Pollen count forecasting. *Immunol Allergy Clin North Am*, 2003. 23(3): p. 423–42.
- Lewis, S. A., et al. Combined effects of aerobiological pollutants, chemical pollutants and meteorological conditions on asthma admissions and A & E attendances in Derbyshire UK, 1993–96. *Clin Exp Allergy*, 2000. 30(12): p. 1724–32.
- Lin, R. Y. and K. D. Williams. Hypersensitivity to molds in New York City in adults who have asthma. *Allergy Asthma Proc*, 2003. 24(1): p. 13–8.
- Linneberg, A., et al. Increasing prevalence of specific IgE to aeroallergens in an adult population: two cross-sectional surveys 8 years apart: the Copenhagen Allergy Study. *J Allergy Clin Immunol*, 2000. 106(2): p. 247–52.

- Lo E and Levetin E. 2007. Influence of Meteorological Conditions on Early Spring Pollen in the Tulsa Atmosphere from 1987–2006. *J. Allergy Clin Immunol* Vol 119 (1) S 101 (abstract).
- Mackowiak, J. The health and economic impact of rhinitis. *Am J Manag Care*, 1997. 3: p. S8–S18.
- Malone, D., et al. A cost of illness study of allergic rhinitis in the United States. *J Allergy Clin Immunol*, 1997. 99(1 Pt 1): p. 22–7.
- Mannino, D. M., et al. Surveillance for asthma--United States, 1980–1999. *MMWR Surveill Summ*, 2002. 51(1): p. 1–13.
- Marion, R., T. Creer, and R. Reynolds. Direct and indirect costs associated with the management of childhood asthma. *Ann Allergy*, 1985. 54(1): p. 31–4.
- McMenamin, P. Costs of hay fever in the United States in 1990. *Ann Allergy*, 1994. 73(1): p. 35–9.
- Melillo, J., et al. Chapter 2: Vegetation and Biochemical Scenarios, in *Climate Change Impacts on the United States: The Potential Consequences of Climate Variability and Change*, Foundation Report. United States Global Change Research Program, Editor. 2001, Cambridge University Press: Cambridge.
- Meltzer, E. O. Quality of life in adults and children with allergic rhinitis. *J Allergy Clin Immunol*, 2001. 108(1 Suppl): p. S45–53.
- Milton, B., et al. The social and economic consequences of childhood asthma across the lifecourse: a systematic review. *Child Care Health Dev*, 2004. 30(6): p. 711–28.
- Mohan, J. E., et al. Biomass and toxicity responses of poison ivy (*Toxicodendron radicans*) to elevated atmospheric CO₂. *Proceedings of the National Academy of Sciences*, 2006.
- Nakagomi T, H Itaya, T Tonsinaga, M Yamaki, SH Isamata, O Nakagomi. *Is atopy increasing?* *Lancet*. 1994. 343(8889): 121–122
- National Center for Health Statistics (NCHS) and C.S. Wilder. Prevalence of Selected Chronic Respiratory Conditions, United States-1970. *Vital and Health Statistics*, 1973. 10(84, DHEW Publication No. (HRA) 74–1511).
- National Center for Health Statistics (NCHS). Current Estimates from the National Health Interview Survey, United States, 1982. *Vital and Health Statistics*, 1985. 10(150, DHHS Pub No. (PHS) 85-1578).
- National Center for Health Statistics (NCHS), P. F. Adams, and V. Benson. Current Estimates from the National Health Interview Survey, 1989. *Vital and Health Statistics*, 1990. 10(176, DHHS Publication No. (PHS) 90-1504).
- National Center for Health Statistics (NCHS) and J.G. Collins. Prevalence of Selected Chronic Conditions, United States, 1986-88. *Vital and Health Statistics*, 1993. 10(182, DHHS Publication No, (PHS) 93-1510).
- National Center for Health Statistics (NCHS), C.S. Wilder, V. Benson, and M. A. Marano. Current Estimates from the National Health Interview Survey, 1992. *Vital and Health Statistics*, 1994. 10(189, DHHS Publication No, (PHS) 94-1517).
- NCHS/CDC. 2001. New Asthma Estimates: Tracking Prevalence, Health Care, and Mortality. [Cited. Available from: <http://www.cdc.gov/nchs/products/pubs/pubd/hestats/asthma/asthma.htm>]
- National Center for Health Statistics (NCHS), et al. Current Estimates of the National Health Interview Survey, 1996. *Vital and Health Statistics*, 1999. 10(200, DHHS Publication No. (PHS) 99-1528).

National Center for Health Statistics (NCHS). 2004. Geographic Region and Division. Updated: December 16, 2004. [Cited 2006 May 9]. Available from: <http://www.cdc.gov/nchs/dataawh/nchsdefs/region.htm>

NHLBI/NIH (National Heart Lung and Blood Institute/NIH). Morbidity & Mortality: 2004 Chart Book on Cardiovascular, Lung, and Blood Diseases. 2004, Washington, DC.

Nielsen, G. D., et al. IgE-Mediated Asthma and Rhinitis I: A Role of Allergen Exposure? *Pharmacology & Toxicology*, 2002. 90: p. 231–242.

O’Connell, E. J. The burden of atopy and asthma in children. *Allergy*, 2004. 59 Suppl 78: p. 7–11.

Patz, J., et al. The Potential Health Impacts of Climate Variability and Change for the United States: Executive Summary of the Report of the Health Sector of the U.S. National Assessment. *Environmental Health Perspectives*, 2000. 108(4): p. 368–376.

Phadia. 2002. Updated: 2002. [Cited 2008 per access to website]. Available from: <http://www.immunocapinvitrosight.com/>

Phipatanakul, W. Allergic rhinoconjunctivitis: epidemiology. *Immunol Allergy Clin North Am*, 2005. 25(2): p. 263–81, vi.

Powell, C. The Delphi technique: myths and realities. *Journal of Advanced Nursing*, 2003. 41(4): p. 376–382.

Powell, R. F. and E. B. Smith. Tumbleweed Dermatitis. *Arch Dermatol*, 1978. 114: p. 751–754.

Prospero JM, Blades E, Mathison G. and Naidu R. 2005. Interhemispheric transport of viable fungi and bacteria from Africa to the Caribbean with soil dust. *Aerobiologia* 21: 1–19.

Puc, M. and M. I. Puc. Allergic airborne grass pollen in Szczecin, Poland. *Ann Agric Environ Med*, 2004. 11(2): p. 237–44.

Puc, M. and T. Wolski. Betula and Populus pollen counts and meteorological conditions in Szczecin, Poland. *Ann Agric Environ Med*, 2002. 9(1): p. 65–9.

Pulimood TB, Corden JM, Bryden C, Sharples L, Nasser SM. 2007. Epidemic asthma and the role of the fungal mold *Alternaria alternata*. *J Allergy Clin Immunol*, 120(3):610–7.

Rasmussen A. The effects of climate change on the birch pollen season in Denmark. *Aerobiologia* 2002; 18:253–65.

Ratard, R. and e. al. Health Concerns Associated With Mold in Water-Damaged Homes After Hurricanes Katrina and Rita -- New Orleans, Louisiana, October 2005. *MMWR*, 2006. 55(2): p. 41–44.

Ray, N. F., et al. Direct expenditures for the treatment of allergic rhinoconjunctivitis in 1996, including the contributions of related airway diseases. *J Allergy Clin Immunol*, 1999. 103(3 Pt 1): p. 401–7.

Reed, S. D., T. A. Lee, and D. C. McCrory. The Economic Burden of Allergic Rhinitis: A Critical Evaluation of the Literature. *Pharmacoeconomics*, 2004. 22(6): p. 345–61.

Reiss, N. M. and S. R. Kostic. Pollen season severity and meteorologic parameters in central New Jersey. *J Allergy Clin Immunol*, 1976. 57(6): p. 609–14.

Rogers, C. A., et al. Interaction of the Onset of Spring and Elevated Atmospheric CO₂ on Ragweed (*Ambrosia artemisiifolia* L.) Pollen Production. *Environmental Health Perspectives*, 2006. 114(6): p. 865–869.

Root, T. L., et al. Fingerprints of global warming on wild animals and plants. *Nature*, 2003. 421: p. 57–60.

- Ross, R. The costs of allergic rhinitis. *Am J Manag Care*, 1996. 2: p. 285–90.
- Rybnicek, O., and S. Jaeger, 2001: Ambrosia (ragweed) in Europe. *ACI International*, 13, 60–66
- Saint Louis County, D. o. H. 2006. Pollen and Mold Center: Elm Family (Ulmaceae Family) - ELM. Updated: 2006. [Cited 2006 May 8]. Available from: http://www.co.st-louis.mo.us/Doh/pollen_site/TreeElm.html
- Schoenwetter, W. F., et al. Economic impact and quality-of-life burden of allergic rhinitis. *Curr Med Res Opin*, 2004. 20(3): p. 305–17.
- Selgrade, M. K., et al. Induction of Asthma and the Environment: What We Know and Need to Know. *Environmental Health Perspectives*, 2006. 114(4): p. 615–619.
- Singer, B. D., et al. Increasing Amb a 1 content in common ragweed (*Ambrosia artemisiifolia*) pollen as a function of rising atmospheric CO₂ concentration. *Functional Plant Biology*, 2005. 32: p. 667–670.
- Smith, D. H., et al. A national estimate of the economic costs of asthma. *Am J Respir Crit Care Med*, 1997. 156(3 Pt 1): p. 787–93.
- Sneller, M. R., H. D. Hayes, and J. L. Pinna. Pollen changes during five decades of urbanization in Tucson, Arizona. *Ann Allergy*, 1993. 71(6): p. 519–24.
- Solomon GM, Hjelmroos-Koski M, Rotkin-Ellman M, Hammond SK. 2006. Airborne mold and endotoxin concentrations in New Orleans, Louisiana, after flooding, October through November 2005. *Environ Health Perspect*, 114(9): 1381–6.
- Stanford, R., T. McLaughlin, and L. J. Okamoto. The cost of asthma in the emergency department and hospital. *Am J Respir Crit Care Med*, 1999. 160(1): p. 211–5.
- Stefanic, E., V. Kovacevic, and Z. Lazanin. Airborne ragweed pollen concentration in north-eastern Croatia and its relationship with meteorological parameters. *Ann Agric Environ Med*, 2005. 12(1): p. 75–9.
- Storms, W., et al. The economic impact of allergic rhinitis. *Allergy Clin Immunol*, 1997. 99: p. S820–4.
- Sutherst, R. W. Global change and human vulnerability to vector-borne diseases. *Clin Microbiol Rev*, 2004. 17(1): p. 136–73.
- Tamarcaz, P., B. Lambelet, B. Clot, C. Keimer and C. Hauser, 2005: Ragweed (*Ambrosia*) progression and its health risks: will Switzerland resist this invasion? *Swiss med. wkly.*, 135, 538–48
- Targonski, P. V., V. W. Persky, and V. Ramekrishnan. Effect of environmental molds on risk of death from asthma during the pollen season. *J Allergy Clin Immunol*, 1995. 95(5 Pt 1): p. 955–61.
- Teranishi, H., et al. Possible role of climate change in the pollen scatter of Japanese cedar *Cryptomeria japonica* in Japan. *Clim Res*, 2000. 14: p. 65–70.
- The Center for Health and the Global Environment, H. M. S. 2005. *Climate Change Futures Health, Ecological and Economic Dimensions*. Updated: November 2005. [Cited 2006. Available from: http://www.climatechangefutures.org/pdf/CCF_Report_Final_10.27.pdf.
- Tidwell, J. 2006. Fall Season Allergy Triggers. [Cited 2006 May 8]. Available from: <http://allergies.about.com/cs/fall/a/aa091399.htm>.
- Tortolero, S. R., et al. Environmental allergens and irritants in schools: a focus on asthma. *J Sch Health*, 2002. 72(1): p. 33–8.

- Tripathi, A. and R. Patterson. Impact of Allergic Rhinitis Treatment of Quality of Life. *PharmacoEconomics*, 2001. 19(9): p. 891–99.
- Troutt, C. and E. Levetin. Correlation of spring spore concentrations and meteorological conditions in Tulsa, Oklahoma. *Int J Biometeorol*, 2001. 45(2): p. 64–74.
- US NHLI. Respiratory diseases: Task force report on problems, research approaches, and needs. Publication No. (NIH) 76–432, E. a. W. Department of Health, Editor. 1972, US National Institutes of Health, Washington, DC.
- Van de Water, P. K., et al. An assessment of projective forecasting of *Juniperus ashei* pollen movement in the Southern Great Plains, USA. *Int J Biometeorol*, 2003. 48(2): p. 74–82.
- Vance, V. and W. Taylor. The financial cost of chronic childhood asthma. *Ann Allergy*, 1971. 29(9): p. 455–60.
- Vazquez, L. M., C. Galan, and E. Dominguez-Vilches. Influence of meteorological parameters on *Olea* pollen concentrations in Cordoba (south-western Spain). *Int J Biometeorol*, 2003. 48(2): p. 83–90.
- Villeneuve PJ, Chen L, Rowe BH, Coates F. 2007. Outdoor air pollution and emergency visits for asthma among children and adults: a case-crossover study in northern Alberta, Canada. *Environ Health*, 6:40.
- Voltolini, S., P. Minale, C. Troise, D. Bignardi, P. Modena, D. Arobba, and A. Negrini, 2000: Trend of herbaceous pollen diffusion and allergic sensitisation in Genoa, Italy. *Aerobiologia*, 16, 245–249.
- Von Hertzen, L. C. The hygiene hypothesis in the development of atopy and asthma-still a matter of controversy? *Q J Med*, 1998. 91: p. 767–771.
- Wan, S.Q., T. Yuan, S. Bowdish, L. Wallace, S.D. Russell and Y.Q. Luo, 2002: Response of an allergenic species *Ambrosia psilostachya* (Asteraceae), to experimental warming and clipping: implications for public health. *Am. J. Botany*, 89, 1843–1846
- Ward, M. M., et al. Lost income and work limitations in persons with chronic respiratory disorders. *J Clin Epidemiol*, 2002. 55(3): p. 260–8.
- Wayne, P., et al. Production of allergic pollen by ragweed (*Ambrosia artemisiifolia* L.) is increased in CO₂-enriched atmospheres. *Ann Allergy Asthma Immunol.*, 2002. 88(3): p. 279–82.
- Weber, R. W. Floristic zones and aeroallergen diversity. *Immunol Allergy Clin North Am*, 2003a. 23(3): p. 357–69.
- Weber, R. W. Meteorologic variables in aerobiology. *Immunol Allergy Clin North Am*, 2003b. 23(3): p. 411–22.
- Weiss, K., P. Gergen, and T. Hodgson. An economic evaluation of asthma in the United States. *N Engl J Med.*, 1992. 326(13): p. 862–6.
- Weiss, K. B. and S. D. Sullivan. The economic costs of asthma: a review and conceptual model. *Pharmacoeconomics*, 1993. 4(1): p. 14–30.
- Weiss, K. B. and S. D. Sullivan. The health economics of asthma and rhinitis. I. Assessing the economic impact. *J Allergy Clin Immunol*, 2001. 107(1): p. 3–8.
- Weiss, K. B., S. D. Sullivan, and C. S. Lyttle. Trends in the costs of asthma in the United States, 1985–1994. *Journal of Allergy and Clinical Immunology*, 2000. 106(3): p. 493–499.
- White, J. F. and D. I. Bernstein. Key pollen allergens in North America. *Annals of Allergy, Asthma and Immunology*, 2003. 91(5): p. 425–435.

- White, J. F., et al. Lack of correlation between regional pollen counts and percutaneous reactivity to tree pollen extracts in patients with seasonal allergic rhinitis. *Annals of Allergy, Asthma and Immunology*, 2005. 94(2): p. 240–246.
- Whitmore, S. E., et al. Aeroallergen patch testing for patients presenting to contact dermatitis clinics. *J Am Acad Dermatol*, 1996. 35(5 Pt 1): p. 700–4.
- Wilson, J. F. Health and the Environment After Hurricane Katrina. *Annals of Internal Medicine*, 2006. 144(2): p. 153–156.
- Wood, S. F. Review of hay fever. 1. Historical background and mechanisms. *Fam Pract*, 1986. 3(1): p. 54–63.
- Ziering, RW and GL Klein. Allergic disease: how to manage three common types. *Postgraduate Medicine*. 1982. 72(2) 163–174.
- Zillich et al. Assessment of the Relationship between Measures of Disease Severity, Quality of Life, and Willingness to Pay in Asthma. *Pharmacoeconomics*, 2002. 20(4): p. 257–65.
- Ziska, L. H. and F. A. Caulfield. Rising carbon dioxide and pollen production of common ragweed, a known allergy-inducing species: Implications for public health. *Australian Journal of Plant Physiology*, 2000. 27: p. 893–898.
- Ziska, L. H., et al. Cities as harbingers of climate change: common ragweed, urbanization, and public health. *J Allergy Clin Immunol*, 2003. 111(2): p. 290–5.
- Ziska LH, George K, Frenz, DA 2007. Establishment and persistence of common ragweed (*Ambrosia artemisiifolia* L.) in disturbed soil as a function of an urban-rural macro-environment. *Global Change Biology*. 13:266–274.