

Inhaler, Anyone? A Study of the Association Between Pollen Levels and Asthma in the Bay Area

ABSTRACT

Asthma is a chronic respiratory condition that affects people globally. Certain environmental factors called asthma triggers cause irritation in the airways and lungs. Commonly identified triggers include particulate matter and other air pollutants. However, asthma is less strongly associated in academic literature with outdoor aeroallergens such as pollen and fungal spore concentrations. Atmospheric concentrations of pollen and fungal spores increase steadily as higher temperatures hasten the beginning of spring, indicating potential future problems with asthma exacerbation. I have compiled studies that look at the relationship between pollen and fungal spores and asthma exacerbations. Asthma exacerbations include people already diagnosed with asthma who experience asthma attacks or other symptoms due to exposure to an asthma trigger. In particular, many studies chose to focus on children (~14 years old). Children represent a vulnerable population to asthma among others examined in various studies. Many of the studies that I included in this literature review have found inconsistent results that are not statistically significant. The lack of strong associations may be due to several factors in the study designs and measurements found in these studies. By examining the weaknesses of these studies, future studies can be designed to more effectively measure the association between aeroallergens and asthma exacerbation.

KEYWORDS

air pollution, literature review, children, particulate matter, asthma trigger

INTRODUCTION

Asthma is a chronic respiratory condition that affects people on a global scale. In the United States alone, 17.5 million adults in 2009 and 7 million children in 2010 were diagnosed with asthma (Pleis, Ward, & Lucas, 2010; Sondik, Madans, & Gentleman, 2011). Not only do asthmatics suffer from the physical symptoms of asthma attacks, but they also suffer in other areas of their lives. For example, absenteeism among asthmatics refers to adults and children at work and school is more prevalent than non-asthmatics due to asthma attacks (Australian Centre for Asthma Monitoring, 2004). These asthma attacks usually begin after an exposure to an asthma trigger (Beggs 1998).

While the exact drivers of asthma remain unknown, certain environmental factors called asthma triggers irritate airways and lungs (Beggs 1998). Extensive research has shown that particulate matter can cause increased asthma incidence and symptoms (Mann et al., 2010; Weinmayr, Romeo, Sario, Weiland, & Forastiere, 2010). Another lesser-known trigger of asthma are aeroallergens (Reid & Gamble, 2009). Pollen is an aeroallergen, an airborne allergy-causing substance that irritates the respiratory system, that leads to health conditions such as allergies and asthma (Bernard, Samet, Grambsch, Ebi, & Romieu, 2001; Gilmour, Jaakkola, London, Nel, & Rogers, 2006). Exposure to higher concentrations of pollen at earlier stages in life increases individual susceptibility to developing asthma later (Pearce, Douwes, & Beasley, 2000; Bjorksten & Suoniemi, 1981). Therefore, one of the potential consequences of higher pollen concentrations is growing asthma incidence (Cecchi et al., 2010). In addition to the increasing number of new cases of asthma, studies suggest that aeroallergens may impact the severity of asthma as well. For instance, a study in Chicago found that the odds of death due to asthma on days with high mold spore counts was 2.16 times greater than on days with lower mold spore counts (Targonski, Persky & Ramekrishnan, 1995). Furthermore, severe symptoms of asthma may prompt individuals to visit emergency rooms. Cases of asthma reported in emergency rooms (ERs) in both Virginia and Texas found that asthmatics exposed to more pollen and fungal spores in their homes were more likely to visit an ER due to asthmatic symptoms (Pollart, Reid, Fling, Chapman, & Platts-Mills, 1998). The relationship between asthma and pollen is important to study as aeroallergen concentrations increase with climate change.

Atmospheric pollen and fungal spore concentrations are steadily increasing as higher temperatures hasten the beginning of spring. Several studies over the last few decades show that plants flower earlier during the spring season. In England, 385 species of plants flowered on average 4.5 days earlier due to increasing average temperatures (Menzel & Fabian, 1999). Other plants also show 3-6 days earlier flowering in the springtime, which suggests a causal relationship between increasing temperatures and earlier onset of spring (Root et al., 2003; Fitter & Fitter, 2002). In an experiment on ragweed pollen, a common allergen and potential asthma trigger, there was 55% higher pollen production resulting from spring conditions starting 30 days earlier than usual.

This study shows the importance of the relationship between the timing of spring and pollen production (Rogers et al., 2006). As temperatures increase, the relationship between aeroallergens and asthma becomes increasingly important to study. However, the literature on aeroallergens and asthma is not as comprehensive and coherent with mixed results.

The lack of strong and consistent studies on aeroallergens and asthma calls for a comprehensive review of the current literature. By analyzing what others have done so far and what they have found, I will examine whether there is an established relationship, or lack thereof, between aeroallergens and asthma exacerbation. Specifically, I will be looking at acute exposures and outcomes rather than long term effects of exposure to aeroallergens. In addition, I will identify vulnerable subpopulations of interest to study for the future.

METHODS

Inclusion and Exclusion Criteria

To determine which studies to use in the review, I set up a series of inclusion and exclusion criteria. When determining the criteria for this review, I considered the exposure and health outcome of interest. Exposure of aeroallergens include pollen and fungal spores. I included studies of all species of pollen and fungal spores as long as they were one of the main exposures in the study. This criteria includes studies of total pollen, specific pollen species, total fungal spores, and specific species of fungi. As for the health outcome, I limited health outcomes to asthma specifically. Any studies looking at "respiratory illnesses" as a

whole without looking at asthma specifically did not qualify. I included all measures of asthma as an outcome including risk ratios, odds ratios, flow expiratory volume (FEV), and others. I did not restrict studies by year conducted, type of study design, or location of study site.

If pollen or fungal spores were included in a study as a confounder with no quantitative result reported, I did not include the study in the review. Similarly, if the study simply concluded that there was "no association" without a quantitative result, I eliminated the study. I also eliminated all studies about indoor exposures to mold. The purpose of this paper is to examine aeroallergens in the air outdoors, which does not include household mold and other indoor spores. Finally, I only used studies that used real data and produced results rather than papers about the hypothetical mechanisms in which aeroallergens irritate the lungs and airways.

Searching the Literature

Because asthma is a health outcome, I mostly used PubMed to find relevant articles. For exposure keywords, I used "pollen," "pollen concentration," "fungal spores," and "aeroallergens." I combined these exposure keywords in different variations with the following outcome keywords: "asthma" and "asthma exacerbation." Many of the initial studies I found indicated frequent use of hospital data for asthma. Therefore, I also added in "emergency department" and "hosp*" to my keyword search. One example of a full keyword search I used is: "pollen" AND "asthma exacerbation" AND "emergency department." Once I found a handful of studies, I also used references in these studies to find further similar studies, eliminating studies of a different exposure (i.e. particulate matter) or different outcome (i.e. cardiovascular disease).

Vulnerable Populations

While I did not initially set out to find specific subpopulations that may be especially vulnerable to aeroallergens, I found that many studies focused on children (ages 0 to 13 or

14). Therefore, I expanded my keyword terms to sometimes include "children." Additionally, I had similar findings with demographic and socioeconomic factors.

RESULTS

Using different combinations of the selected keywords, I found 31 potential studies. Of these studies, I excluded 14 of them. Despite using specific keywords, some studies were about pollen and allergies, pollutants and asthma, or weather and asthma. Each of these categories has either a different exposure or outcome variable than what I was trying to find.

Some studies used exclusively pollen or fungal spores as the exposure while others had both in their analysis. The following tables summarize the main statistics from each paper. Table 1 summarizes findings on pollen and asthma, while Table 2 summarizes findings on fungal spores and asthma. Some studies can be found in both tables.

Table 1. Summary of Pollen Statistics.

Author, Year of Publication	Study Design/ Statistical Analysis	Exposure	Results	Location
Anderson, et al. 1998	time series	Birch pollen	0.78 (0.15 - 1.42) 0.90* (0.14 - 1.67) % increase in daily asthma admissions	London, England
Burr, et al. 2003	ecological analysis	Grasses Total pollen	-0.0004* (p-value 0.29) -0.0802* (p-value 0.18) Regression coefficient	Worldwide data
Dales, et al. 2000	time series	Weeds Grasses Trees	1.85 (SE 1.23) 0.4 (SE 0.82) 0.44 (SE 0.89) % increase emergency asthma visits	Ottawa, Canada

Epton et al. 1997	1 year prospective study	Conidia Total pollen	0.84 (0.72 - 0.98) 0.93 (0.83 - 1.04) Rate ratio of high symptom days	Blenheim, New Zealand
Halonen et al. 1997	longitudinal prospective study	Bermuda grass Olive tree Mesquite tree Careless weed Mulberry tree	0.5* (0.3 - 0.9) 6 yr-olds 1.8* (0.8 - 4.0) 11 yr-olds 0.9* (0.5 - 1.6) 6 yr-olds 1.4* (0.7 - 3.2) 11 yr-olds 0.9* (0.4 - 1.7) 6 yr-olds 1.0* (0.4 - 2.3) 11 yr-olds 1.8* (1.1 - 3.1) 6 yr-olds 0.4* (0.2 - 1.0) 11 yr-olds 1.8* (0.9 - 3.6) 6 yr-olds 1.6* (0.6 - 4.6) 11 yr-olds Odds ratio for asthma	Tucson, Arizona
Hanigan & Johnston 2007	time series	Total pollen	41.42 (-20.94 - 153) % change in relative risk for emergency admissions	Darwin, Australia
Heguy, et al. 2007	time series	Ragweed Grasses Weeds	0.19* (-0.35 - 0.73) 2.06* (0.58 - 3.57) 0.23* (-0.17 - 0.62) % change in emergency department visits	Montreal, Canada
May, et al. 2010	time series	Tree pollen	0.458 (0.152 - 0.765) Correlation coefficient	Washington, DC
Targonski, et al. 2007	logistic regression	Tree pollen Grass pollen Ragweed	0.99 (0.90 - 1.09) 1.34 (0.89 - 2.02) 0.72 (0.45 - 1.15) Odds ratio	Chicago, Illinois
Tobias, et al. 2004	time series	Olea Plantago	-19.8 (-39.7 - 6.6) 31.3 (-0.8 - 73.8)	Madrid, Spain

		Poaceae Urticaceae	78.7 (34.6 - 137.2) 49.8 (14.2 - 96.4) % change in risk for emergency room visit	
Zhong, et al. 2006	time series	Oak/maple Pinaceae Ragweed	23* (2 - 49) 34* (24 - 45) 54* (2 - 133) % increase in daily asthma visits	Cincinnati, Ohio

Bold: statistically significant

*Result for children

Table 2. Summary of Fungal Spore Statistics.

Author, Year of Publication	Study Design/ Statistical Analysis	Exposure	Results	Location
Atkinson, et al. 2006	time series	Total spores	1.06* (0.94 - 1.18) Relative risk for increase in visit to hospital	London, England
Cakmak, et al. 2004	time series	basidiomycetes	9.3* (4.8 - 13.8) % increase asthma admissions, males < 13	10 Canadian cities
Dales, et al. 2000	time series	Deuteromycetes Basidiomycetes Ascomycetes	1.94 (SE 0.9) 4.10 (SE 1.63) 2.77 (SE 1.0) % increase emergency asthma visits	Ottawa, Canada
Epton et al. 1997	1 year prospective study	Ascospores Basidiospores	1.00 (0.87 - 1.16) 1.19 (0.97 - 1.46) Rate ratio of high	Blenheim, New Zealand

			symptom days	
Halonen et al. 1997	longitudinal prospective study	Alternaria	2.3* (1.4 - 3.6) 6 yr-olds 2.7* (1.2 - 6.0) 11 yr-olds Odds ratio for asthma	Tucson, Arizona
Lopez et al. 1989	Bronchial challenge for selected individuals	Basidiospore	20 - 40% decrease in flow expiratory volume	New Orleans, Louisiana
Neas, et al. 1995	prospective study	Cladosporium Epicoccum Ganoderma Xylaria	-1.03* (-1.86 - -0.20) -1.50* (-2.83 - -0.18) 1.53* (-0.36 - 3.43) -0.49* (-1.87 - 0.90) % change in flow expiratory volume	State College, Pennsylvania
Raphoz, et al. 2010	time series	Ganoderma Deuteromycetes Cladosporium	-0.40* (-0.77 - -0.4) -0.17* (-0.27 - -0.07) -0.20* (-0.33 - -0.06) % change in emergency asthma visits	Montreal, Canada
Targonski, et al. 1995	logistic regression	Total spores	1.17 (1.05 - 1.31) Odds ratio	Chicago, Illinois

Bold: statistically significant

*Result for children

Less than half of the pollen studies and two-thirds of the fungal spore studies showed statistically significant results. Interestingly, Raphoz, et al. found statistically significant negative association between fungal spores and asthma in Montreal, Canada.

DISCUSSION

Overall, pollen concentrations showed an inconsistent relationship with asthma. Some studies showed a positive, statistically significant association, while others had wide confidence interval ranges. Fungal spores, while still not unanimous, showed a slightly stronger association with asthma. However, both aeroallergen exposures demonstrated inconsistency and lack of statistical significance. It is possible that the lack of statistical significance in these studies indicates no real relationship between aeroallergens and asthma exacerbation. However, it is difficult to determine this statement concretely without more rigorous and thorough studies on the matter.

Common Study Design Limitations

Many of the studies found inconclusive or statistically insignificant results for the association between aeroallergens, especially pollen, and asthma exacerbation that may be due to limitations in the study designs. First, all of the studies had a limited population size. In many studies, the small study population is due to the focus on one hospital, limiting the size of the study population. In addition, the studies had limited number of days in the study. Even the longer studies were around one year long, which is not enough time to capture the trends and seasonality in either aeroallergens or asthma exacerbation. Because levels of pollen and fungal spores as well as asthma hospitalizations vary by year, it is important to capture more than one year in a study.

Another related limitation of the studies that used hospital data is a low mean number of admissions per day. Asthmatics do not visit the emergency room or their physician every day for symptoms. As a result, there may be several days without admissions countered by days of high admissions. Taking the average of these extremes can dilute the effect of days with high admissions. Therefore, all of these limitations combined dilute the effect of aeroallergens, leading to statistically insignificant results and large confidence intervals. A reasonable solution to these problems is to increase population size by expanding the area studied and by studying the area for a longer period of time.

Temporality of Aeroallergens and Asthma

Another reason for large confidence intervals and lack of statistical significance may be due to a mismatching seasonality of asthma and aeroallergens. Specifically, pollen tends to peak in the spring and fall depending on the species. These peaks tend to be very distinct regardless of location in the world. Similarly, fungal spores also have peaks at similar times, but these peaks are less pronounced. These trends prove to be consistent through the years (Reid and Gamble 2009). On the other hand, asthma increases during the winter. Colder weather leads to concurrent illnesses such as pneumonia that can exacerbate asthma. Therefore, aeroallergen levels increase right before and after a common increase in asthma hospitalizations. At a cursory glance, it seems as though pollen and fungal spores may have a protective effect against asthma, which is highly unlikely. Without careful analysis taking these trends into account, it is easy for risk ratios and other measures to become statistically insignificant. This reason may explain why Raphoz et al. found a statistically significant protective effect of fungal spores.

Vulnerable Populations

Around half of the studies either focused solely on children or purposely calculated separate risk estimates for children within their larger study. Children are a susceptible and sensitive group to aeroallergens. They spend more time outdoors than adults, exposing themselves more frequently to outdoor air pollution. In addition, children take in 20% to 50% more air during physical activities than adults (Kleinman, 2000). The summarized results shown in Tables 1 and 2 also show that many of the risk estimates for children tend to be more strongly positive than estimates for the general population.

In addition, the Cakmak et al. study from 2005 indicates that while there is no difference in risk between different ethnicities, education attainment by area does. In neighborhoods of overall lower educational attainment in Canada, the association between pollen and molds and asthma hospitalization was stronger. Therefore, demographic and socioeconomic variables may become useful in identifying vulnerable populations such as areas with low educational attainment.

Limitations

Of course, there were also some limitations in my literature review of this topic. Due to the varying measures ranging from relative risk to flow expiratory volume, I was unable to calculate an overall effect estimate from the conclusions of all the studies together. Therefore, rather than reporting a conclusive overall number of what current literature suggests, I can only analyze the patterns and commonalities from these studies. Additionally, due to the small volume of literature that I could find for specific regions, I accepted studies from all over the world. These scattered locations represent various climates, healthcare systems, and other demographic features that make results difficult to compare directly. Future studies conducted in similar regions or types of climates may reveal more concrete associations between specific species of pollen and fungal spores and asthma for those areas.

Future Directions and Broader Implications

Based on this literature review, I believe that more research on this topic is needed to draw conclusive evidence of an association, or lack thereof, between aeroallergens and asthma. I believe an ideal study for the future would be a time series analysis that studies a period of at least five years. So far, studies have only looked at one to two years, so five years may show a better balance between the years studied and contribute to statistical significance. An effective study should also be able to take into account the mismatched seasonality between the exposure (aeroallergens) and the outcome (asthma). This consideration could perhaps be achieved by analyzing the different seasons separately.

For example, I believe that Fresno, California would be an ideal study site for analysis. This unique environment encompasses both urban and agricultural environments and exposures unlike many of the previous studies. Exposure measurements would be daily concentrations of pollen and fungal spores. Based on the Figure 1, Fresno seems to follow the predictable pollen peaks in the spring and fall, which means that the results from this study could possibly be extrapolated to similar regions.

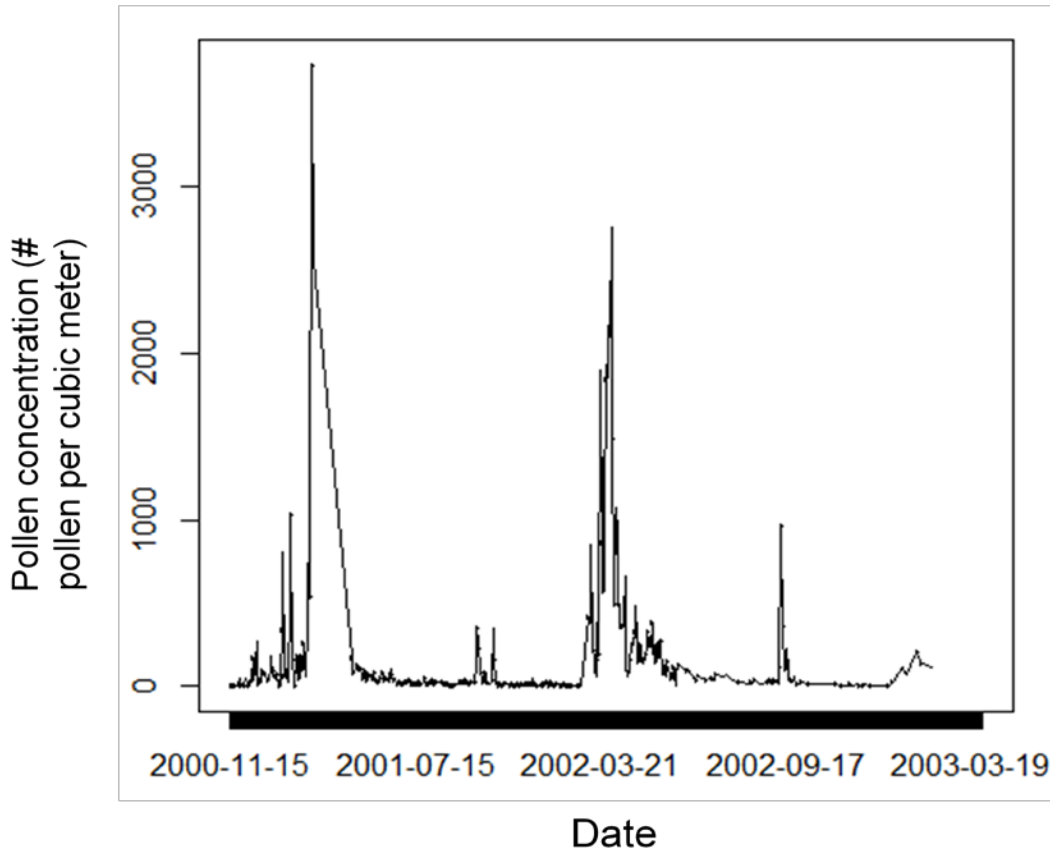


Figure 1. Total pollen concentration in Fresno, CA 2000 – 2003.

To measure asthma exacerbation, I would use daily emergency room visits as well as hospitalizations due to asthma to cover all patients during the day who experience any asthma exacerbation symptoms. Based on studies in this literature review, I would also factor in other meteorological variables including wind, temperature, and humidity. Finally, an analysis of vulnerable populations within the city would clarify whether children or people of certain demographic and socioeconomic statuses are at higher risk of asthma exacerbation due to aeroallergens.

If there is an association found between pollen levels and incidence of asthma, then this information can be used for public health initiatives tailored for the Bay Area. First, hospitals and healthcare providers in the most affected regions can prepare for patients with asthma using the projected increases in the number of cases of asthma. Preparations may include stocking up on supplies and treatment medications or training nurses and doctors to handle cases of asthma (Balbus and Malina 2009). In addition, populations identified as high

risk for asthma due to pollen levels in their areas can be notified and educated about asthma symptoms and managing these symptoms. Because asthma is a disease especially burdened on children, education at early ages can be crucial. Hopefully, education will reduce visits to the emergency room by decreasing the severity of symptoms through self-regulation (Flores et al 2009). Finally, a positive association between aeroallergens and asthma could result in more thorough screening in children and adults for asthma during regular check-ups and emergency room visits. In light of climate change, drawing conclusive evidence of an association between aeroallergens and asthma can help better prepare us for health problems, especially in young children, in the future.

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