Outdoor aeroallergens in asthma exacerbations

Role of outdoor aeroallergens in asthma exacerbations: epidemiological evidence

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Confounding factors complicate the interpretation of time series studies in examining the role of outdoor aeroallergens in asthma exacerbations

Despite historically low levels, outdoor environmental pollutants such as nitrogen dioxide, sulphur dioxide, and particulate matter are thought to play a role in exacerbating asthma. Much of this evidence comes from ecological ''time series'' studies that use sophisticated statistical methods to examine temporal associations between daily counts of asthma attacks and daily levels of air pollution at the *population* level. A good example of this type of study is the multi-city European study APHEA (Air Pollution and Health: an European Approach).[1 2] Panel studies have also investigated temporal associations between daily outdoor air pollution levels and asthma but use the symptoms, lung function and medication use of *individuals* as the health status indicators. The multi-city equivalent in panel design is the PEACE study (Pollution Effects in Asthmatic Children in Europe). However, it failed to find statistically significant associations between particle measures, sulphur dioxide and nitrogen dioxide and respiratory symptoms, peak expiratory flow and medication use.[3]

Only a relatively small number of studies have used the time series approach to investigate the health effects of aeroallergens at the population and individual levels. Some studies of air pollution have included pollens and fungal spores as potential confounders,[4–7] while others have been designed specifically to investigate the health effects of aeroallergens.[8–16] The conclusions from this latter group are inconsistent—some report significant effects of pollens and spores and others do not. This inconsistency may be because there is no real association or because of methodological problems associated with this type of study.

METHODOLOGICAL PROBLEMS WITH TIME SERIES STUDIES

Pollen distribution

One methodological problem faced by researchers using time series designs is that the appropriate exposure-response curve for an effect of aeroallergens on asthma exacerbations is not known. Many pollen species have defined seasons, with high counts during these seasons and none for the remainder of the year. Their skewed distributions present the analyst with particular statistical challenges. One approach is to divide study days into groups defined by the percentiles of the pollen or spore distribution. At its simplest level, this approach can examine the health effects of aeroallergens by comparing days with zero aeroallergen counts with days with non-zero counts. By subdividing the study days into more groups, the method can reveal possible threshold values. For example Lewis *et al*[11] examined the linearity of the effect of aeroallergens by dividing the daily counts of A&E visits and admissions for asthma by tertile of aeroallergen counts plus a further group for days when counts were zero. They found stronger effects of grass pollens on days above the third tertile (when accompanied by thunderstorm activity). A similar finding was made by Salvaggio and co-workers.[14] Newson *et al*[17] found that the number of epidemics of asthma was over-represented on high pollen days (>50 grains/m^3 per day) compared with low pollen days or days with zero pollen counts. However, Dales *et al*[8] assessed the linearity of the effect of pollen counts (classified as weeds, grasses and trees) on emergency visits for asthma to a children's regional hospital in Ontario and found no evidence for non-linearity. Whereas it is important to explore possible departures from a linear concentration-response relationship, individual studies quoting a specific threshold of effect should be interpreted with caution because such analyses are often ''post hoc'' (or data driven).

Meteorological conditions

Meteorological conditions may also contribute to the apparent inconsistencies in the results of time series studies of the health effects of aeroallergens. The weather may act as an effect modifier by interacting with aeroallergen levels. Salvaggio and colleagues[14] studied admissions for asthma in New Orleans in relation to total spore and pollen counts at three different levels of humidity. They found that the percentage of high asthma admission days increased on days with low or intermediate levels of humidity but not on days of high humidity. In a synoptic evaluation of asthma hospital admissions in New York, Jamason and coworkers[10] found that the impact of weather conditions varied according to season (greatest effect in autumn and winter), although they found no evidence of an effect of pollen on asthma admissions in any season.

Meteorological conditions may also have a significant *indirect* role on asthmatic subjects by permitting the clearance or build up of outdoor allergens.[10] In most ecological time series studies of asthma exacerbations and environmental factors (aerobiological and air pollution) a *direct* effect of the weather is studied. Temperature and relative humidity are the most common measures although others also include rainfall, barometric pressure, and wind speed and direction. Low temperature[18] and relative humidity[8 18 19] are most commonly associated with independent effects on asthma admissions. The evidence for an effect of rainfall is mixed.[9–13 18] For instance, thunderstorms have been associated with asthma epidemics.[17–19 20–23] One possible explanation is that the humidity preceding a thunderstorm, or rainfall during a thunderstorm, leads to the break up of pollen grains releasing starch granules that are then circulated (together with fungal spores if present) by the exceptional meteorological conditions.[24]

Air pollution

The possible role of air pollution in confounding or modifying the effects of pollen is of particular interest. A number of studies have investigated the possibility that pre-exposure to air pollution sensitises individuals to the effect of aeroallergens.[25–29] These clinical studies have not been supplemented by many epidemiological studies. Lewis *et al*[11] examined possible interactions between air pollution and both pollens

and spores but failed to find evidence for a synergy between these environmental factors in causing daily asthma admissions and A&E attendances in Derbyshire, UK.

Coincident aeroallergen exposure

Similar seasonal patterns for aeroallergen species can make it difficult to disentangle the separate health effects of individual pollens or spores. The co-linearity in the statistical model prevents any one factor being identified as the causative agent and also can lead to an underestimation of the potential health effects. This is well illustrated by a recent study by Tobias *et al*.[16] Their data showed two clearly defined peaks in the daily number of admissions for asthma that coincided with spikes of high concentrations of *Poaceae* and *Plantago* in the atmosphere. However, in one of the years studied both pollens reached concentrations above the 95th percentile (only just for *Poaceae*), but without a noticeable effect (by eye) on asthma admission numbers. Heavy rain during the pollen season was thought to have suppressed both the size of the pollen peaks and their duration.

CONCLUSIONS

The paper by Tobias and colleagues is important because it suggests that exposure to (grass) pollen in the atmosphere can have serious health effects for asthmatics. However, evidence from other studies has been less striking. The size of any health effect and the existence of a threshold in the pollen concentration at which this effect is triggered are not clear. The possible roles of meteorological conditions and other environmental factors in determining the nature of any health effects of pollens are not fully understood, although it seems that thunderstorms in particular are associated with striking epidemics of asthma in which aeroallergens may play a role. Further studies in other locations with different environmental situations are required to provide the variability in confounding factors and coincident exposures in order to clarify which aeroallergen species can have a detrimental effect on the health of asthmatics and under what conditions.

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Competing interests

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Further details on the competing interests of the author of the above editorial and the COPD guidelines committee can be found on the *Thorax* website (http://thorax.bmjjournals.com/cgi/content/full/59/3/181/DC1).