SPRINGTIME ASTHMA HOSPITALIZATIONS AND POLLEN LEVELS : ARE THEY RELATED ?

by

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ABSTRACT

Asthma morbidity has previously been shown to peak in the spring and the autumn in Ontario and elsewhere. The cause of these peaks has not yet been established. Coincident with the spring peak, trees and grasses pollinate in Southern Ontario. Although it is known that pollen allergen can exacerbate asthma, it remains to be shown that there is a relation between pollen levels and asthma hospitalizations during the spring. In this ecological study hospital emergency admissions in London, Ontario were examined during the peak spring months of the years 1983-88 to determine if they were associated with tree and grass pollen levels. Pollutants and weather factors were also analyzed because they may have confounded the association between asthma and pollen, or may have had their effect modified by pollen. Asthma admissions in London during this study showed spring and fall peaks similar to what has been described elsewhere. Although asthma peaked between April and June of each year the exact month varied from year to year. Tree pollen peaked each April or May and grass pollen peaked each June. Daily and weekly asthma admissions were associated significantly with tree pollen (r_s = 0.12 and 0.25 respectively) and total pollen (tree + grass) counts (r_s = 0.12 and 0.34 respectively) but not with grass pollen alone. The same associations were found using ANOVA after the pollen was categorized into quartiles. These associations stood-up after controlling for confounders. A negative associations of asthma admissions was also

found with temperature and this became stronger when pollen counts were elevated. Although negative associations were found for asthma with NO_3 and SO_4, these associations are not plausible and may be due to confounding by temperature. The ecological nature of this study prevented ascertainment of exposure and precluded controlling other potential confounders. Therefore, although they are important, it can not be concluded that the associations in this study are causal.

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A. INTRODUCTION:

Asthma is a common disorder which carries the risk of significant morbidity and premature mortality[1]. In 1987 it was noted that both morbidity and mortality rates for asthma in Canada had been increasing[2]. Between 1970-72 and 1980-82 hospitalization rates rose by 50 percent, while death rates rose by 9 percent in males and 44 percent in females. Although half a million Canadians were estimated to have asthma[3] in 1978/79, a study from Montreal in 1986 suggests that, at least in children, the prevalence of this disorder is rising[4].

Asthma Seasonality.

One of the most striking aspects of asthma epidemiology is the tendency for morbidity from this disease to display seasonal periodicity. This tendency was first noted by Hippocrates in the writings of his third Aphorism:

> "All diseases occur at all seasons of the year, but certain of them are more apt to occur and be exacerbated at certain seasons...."[The diseases] of autumn [are].....asthma."[5]

In more recent years, Mao et al[6] have observed that asthma morbidity in Ontario, Canada follows a seasonal pattern. They noticed this while examining hospital separation data from the Hospital Morbidity Records Institute (HMRI) for the years 1978/80-1986/87. For persons aged 15-34, two annual peaks in asthma hospital admissions were found: a smaller peak during the spring (April-May) and a larger peak during the auturnn (September-October).

This seasonal periodicity has been noticed in other countries as well. In Britain, hospital admissions for childhood asthma increased by 20-25% in May through July and by about 40% in September through October during the years 1975-81[7]. In the United States, asthma hospitalizations in the 5-34 age group showed a slight increase in March and a larger increase in the autumn during the years 1982-86[8]. Spring and autumn increases in asthma hospital admissions have also been noted in Israel[9] and in Hong Kong[10].

The reason for these spring and autumn increases has not been determined but suggestions centre around environmental factors[6,7,8]. If an environmental factor did play a role, it should have the potential to clinically exacerbate asthma and have an element of ubiquity such that many individuals could be affected simultaneously. The factor should also vary by season and show changes at the time of year when asthma peaks.

POLLEN AND THE SPRING ASTHMA PEAK.

Asthma spring peak coincides with pollination.

A factor that could play an important role in driving spring asthma admissions is pollen. During the spring large quantities of airborne pollens are released into the atmosphere in Southern Ontario[11,12]. A tree pollen season extends from late March to mid June, and grass pollinates from the end of May to mid July.. After they are released, pollens can travel large distances in air currents[12]. Some of these pollens are highly allergenic[11] and, in conjunction with their dispersal in the air, they have the potential to affect many sensitized individuals.

The ability of pollen to exacerbate asthma.

Allergenic mechanism. Allergen extracted from pollen grains is able to acutely exacerbate asthma. This has been demonstrated by Boulet[13] who administered aerosolized ragweed pollen extract via mask to nine volunteer asthmatics who were sensitized to ragweed pollen. The forced expiratory volume in 1 second (FEV1) fell by 20 percent in these subjects immediately after inhaling the allergen. As well, 5 of

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[*] Tree pollination usually starts in March with elm, alder, maple, poplar, aspen, birch, ash, mulberry, and willow. Elder, beech, sycamore, hackberry, oak, mulberry, walnut, and hickory follow starting in April. Tree pollination is generally finished by mid June. Grass pollinates from mid May and to mid July. It is difficult to differentiate between individual grass species pollen but bluegrass, orchard grass, timothy, and red top dominate. In the late summer and early autumn, ragweed pollinates.

the 9 subjects demonstrated a further, secondary fall in the FEV1 at 4 to 8 hours post exposure.

However, even though pollen *allergen* can exacerbate asthma, pollen *grains* probably do not gain access to the lower airways in any appreciable numbers[14]. Large pollen grain diameters (25 to 40 μm[12]) would make it difficult for them to pass upper airway defences.[15,16]. Thus it would seem that smaller pollen fragments would be necessary to deliver allergen to the smaller airways in the lung. Solomon et al[17] have shown that such small allergenic components do in fact exist. They sucked air containing ragweed pollen (20 μm diameter) through a 5 μm filter and found that ragweed pollen allergen passed through the filter on to a collection sheet placed on the other side.

Further evidence that pollen allergen is related to asthma has been provided by measurements of IgE antibody levels from the sera of asthmatics. This was done on 59 randomly selected asthmatics[18] who presented at David Grand Medical Center emergency room in northern California during the spring when ryegrass pollen was present. IgE antibodies to a total of 5 allergens - mite, cat, cockroach, ryegrass pollen, and ragweed - were assayed in the subjects' sera. Comparison was made with

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* Particles greater than 10 um are trapped in the upper airways by 3 mechanisms: Impaction, sedimentation, and diffusion. Impaction occurs in the nose and at tracheal and bronchial bifurcations. Sedimentation and diffusion of particles from air to the wall of airways occurs as a result of diminishing air velocity as the airways branch out.

the sera of 59 control non-asthmatic subjects during the same period. 92 percent of the asthmatics had elevated IgE antibodies (greater than 200 units) against ryegrass pollen compared with only 14 percent of the non-asthmatic subjects (chi-square = .69, $p < 0.0001$). There was, however, no significant difference in IgE antibody levels for any of the other allergens between the two groups.

Nonallergic bronchial hypersensitivity. As well as inducing an allergic response, exposure to pollen or pollen allergens can cause the airways of asthmatics to become more responsive to other factors[19] such as pollutants, irritants, and temperature. This phenomenon is known as **increased nonallergic bronchial responsiveness**[20,21]. Boulet et al[13] studied thirteen ragweed sensitive asthmatics and found that nonallergic bronchial responsiveness was significantly increased during the ragweed season compared with immediately before the season started..

Other aeroallergens. Mould spores such as *Alternaria* and *Penicillium* can initiate acute attacks of asthma[22]. However fungal spores do not have a straightforward,

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• Nonallergic bronchial responsiveness is commonly assessed by PD_{20} methacholine. This is the provocation dose of methacholine that is required to cause a 20 % fall in the (FEV1). If the bronchial tubes are nonspecifically responsive, lower dose of methacholine are required to reduce the FEV1.

brief spring-time season, tending rather to be present much of the year except when snow is present[11]. Allergens from dust mites are able to exacerbate asthma[23]. These allergens however tend to be high in the months August to December and lower during the spring[24].

Thus there is circumstantial evidence which suggests that pollen might play a role in increasing asthma admissions during the spring. Firstly, tree and grass pollination grossly coincides with the spring-time increase in asthma admissions. Secondly, pollen has the potential to exacerbate asthma. However if pollen is responsible for the increase in admissions during the spring it should be possible to demonstrate that asthma admissions are related to pollen counts.

Are asthma admissions related to pollen levels?

The most detailed study to date comparing aeroallergens levels with asthma was carried out in New Orleans by Salvaggio et al[25]. They recorded daily adult asthma admissions to Charity Hospital during the months June to December in 1967 and 1968. These were compared with daily pollen and mould spore counts that were measured using a sampler located in the center of the city on top of the university medical buildings. Analyses were done in contingency tables comparing "epidemic" asthma admission days (upper one third of all days) with high total mould and high total pollen counts (upper one third). When total pollen and moulds were considered together, high counts were significantly associated with "epidemic" asthma days ($p < 0.01$) over the full study period. However, when pollen was considered alone (without moulds), the association with asthma admissions was not present over the full study period: high pollen counts were associated with epidemic days only during the months August and September (the months that ragweed pollinates) and only if the upper one third cutpoints for pollen were recalculated each month. Thus although crude associations between asthma admissions and pollen and spore counts were found in this study, springtime asthma and the importance of springtime pollens (trees and grasses) were not addressed. It must also be noted that this study did not consider the possibility of confounding by other environmental variables.

Other studies have looked for associations between asthma admissions and aeroallergens and found varying results. The only major Canadian study to date which has addressed this question was carried out in Hamilton Ontario by Levy et al[33]. They reviewed coded charts of all patients admitted to the 4 hospitals in Hamilton and selected out admissions for acute respiratory illnesses (bronchitis, bronchiolitis, emphysema, pneumonia, and asthma) from July 1970 until July 1971. These admissions were compared with pollen counts, as well as pollutants, and weather measurements. *No association* was found between respiratory admissions and pollen levels. However, asthma admissions were not analyzed separately from other respiratory diseases in this study. It must also be noted that pollutants were the main thrust of this study and there were no details of what pollens were considered or on the methods used to collect the grains.

A study carried out in Brighton, U.K., looked at asthma admissions in young children only[26]. During the period August 1982 to November 1983, the number of daily asthma admissions for children under 18 months of age to Royal Alexandra Hospital for Sick Children was compared with biometeorological factors. Weather variables - wind speed, wind direction, relative humidity, barometric pressure, temperature, and rainfall - were measured at the local meteorological measuring station 5 miles from the hospital. Biological particles were measured using a volumetric spore trap on the hospital roof. These counts included pollen, green algae and fungal spores. Pollutants were not considered in this study. Analysis was done by fitting Poisson regression models. Factors that were significantly related to admissions included wind direction ($p < 0.001$), barometric pressure ($p < 0.005$), rain ($p < 0.001$), Basidiospores ($p < 0.001$), and green algae ($p < 0.005$). Although no relationship was found between asthma and pollen, only grass pollen was analyzed in this study. There was no discussion of what other types of pollens (trees, weeds) might have been present and whether these might have had an effect on asthma admissions. Furthermore, the study spanned a full 16 months. Grass pollen would have been present during only a few of these months and would not be expected to show an effect on asthma admissions over the full 16 months. For these reasons the lack of an association between pollen and asthma in this study may not be valid.

In Kuwait, emergency room visits of asthmatics between the ages of 1 and 12 at Mubarak-Al Kabeer Hospital were studied during the period July 1982 - June 1985[27]. It was found that asthma visits were highest during the winter months (December - January) and lowest during the summer. Pollen in Kuwait - which is dominated by the Mesquite tree - characteristically shows a bi-annual distribution, peaking in August/October and April/May. Therefore, because the seasonal pattern of pollen was noted to be different from that of asthma visits, it was argued that the two could not be related. However, no formal statistical testing was done in this study.

In Los Angeles the daily number of children presenting to the emergency room of Childrens Hospital of Los Angeles were tabulated during the six month period from August 1, 1979 to January 31, 1980[28]. These visits were then compared with airborne allergen data, pollutants and meteorological variables. Allergens were measured at a location in Beverly Hills and included alternaria, elm, oak, walnut, grass, ragweed, and sage. However, only the total allergen count (sum of all these species) was analyzed in the study. Unfortunately, the allergens were measured only biweekly and these biweekly measurements were used to estimate the values on days for which measurements were not made. A significant association was found between these estimated allergen measurements and daily asthma visits ($r= 0.24$, $p < 0.01$) over the six month period of this study. However the validity of these results must be questioned because of the methods used.

A study in northern California looked for an association between grass pollen and both asthma emergency room visits and asthma hospitalizations[29]. The study was carried out at the David Grant USAF Medical Center between January 1981 and December 1984. Asthma emergency room visits included all visits to the emergency room for physician diagnosed asthma. Asthma hospitalizations included all admissions that were coded asthma (extrinsic, intrinsic or unspecified) on the discharge summary. Aeroallergen counts were performed using a gravity collector on the roof of the medical center. Temperature, barometric pressure, and wind speed were also measured and compared to asthma visits. Total monthly grass pollen counts showed a strong positive correlation with monthly asthma emergency room visits ($r = 0.90$, $p < 0.001$) and with monthly asthma hospitalizations ($r = 0.72$, $p < 0.001$). Other aeroallergens' counts were minuscule compared with grass pollen counts in this region and were therefore not presented in the study. Weather variables showed no association with asthma. Although a significant association was found between grass pollen and both asthma emergency room visits and asthma hospitalizations, this study analyzed only on a monthly basis rather than considering a weekly or daily scale, thus increasing the possibility of spurious correlations. Furthermore, there was no control for other potential confounding environmental variables in this study.

Thus there is some evidence to suggest that asthma admissions are related to pollen levels. Most noteworthy is Salvaggio's finding of an association between pollen and asthma admissions in New Orleans during August and September. However an association between pollen and asthma admissions during the ***spring*** on a daily or weekly basis needs to be established. Furthermore, a major shortcoming of previous work has been the failure to consider the potential for confounding by other environmental factors.

THE POTENTIAL FOR CONFOUNDING BY OTHER ENVIRONMENTAL FACTORS.

When looking for an association between pollen levels and asthma admissions, other environmental factors including weather and pollutants[30] must be kept in mind. It is possible that some of these factors may be related to both pollen levels and to asthma admissions. If this is the case, confounding by these factors must be ruled out.

Relation of environmental factors to pollen.

Ambient Pollutants: The exact relationship between pollens and pollutants has not been determined. Both, however undergo changes during the spring raising the potential for covariation. During the spring when pollen levels are increasing a number of ambient pollutant levels also rise, while other pollutants decline. The pollutants that rise include sulphates (SO_4^{2-} and H_2SO_4), nitrates (NO_3), and ozone (O_3)[31]. These are secondary pollutants which are produced through photochemical oxidation of primary combustion products. As the amount of sunlight increases during the spring, this photochemical oxidation increases. Ozone is particularly stable and can be transported over great distances by wind[31].

Levels of primary combustion products on the other hand tend to decrease during the spring as a result of photochemical oxidation. These pollutants include sulphur dioxide (SO_2) and nitrogen dioxide (NO_2). SO_2 is produced through the burning of sulphur containing fuels (coal, oil), the smelting of sulphur containing ores. and the refining of petroleum. NO_2 is mainly produced from automobile emissions. NO_2 levels are thus extremely variable and depend on proximity of sources (eg highways).

Levels of fine particulate matter are, like pollen dependent on weather factors such as wind[30]. Thus under some weather conditions their levels may follow patterns similar to pollen.

Weather: Meteorological factors directly relate to plant pollination. Cool temperatures reduce or completely inhibit pollination[12]. High wind speeds increase the amount of pollen that is released from a mature flower at any given time[11,12]. Maximal pollen concentrations in the air are attained at wind speeds of 13 to 17 miles per hour[11]. Lower humidity also favours pollen release and rainfall may both inhibit pollen release and wash airborne pollen out of the atmosphere[11].

Associations with asthma admissions:

In order to confound the association between pollen and asthma admissions, environmental factors should themselves be associated with asthma admissions. Past ecological studies have looked for associations of asthma hospitalizations with pollutants and weather measurements.

Pollutants: There have been three Canadian studies which have looked for associations between asthma hospital admissions and ambient pollutant levels. As well there have been several other recent studies in other parts of the world.

Firstly, Bates & Sitzo[32] studied daily hospital admissions recorded by the Ontario Health Insurance Programme at 79 hospitals extending over the region between Windsor and Peterborough, Ontario during the years 1974 and 1976-1983. Admissions were only studied for the months of July/August and January/February. Daily admissions were grouped into total, respiratory, respiratory minus asthma,

asthma and non-respiratory. Daily air pollution data was obtained from 17 sampling stations across the region and weather was measured at one station in the centre of the region. Pearson correlation coefficients were calculated between pollutant levels and deviations of admissions from the mean admissions for the same day of the week, the same year, and the same season. *During July and August* significant correlations were found for asthma admissions with O_3 ($r = 0.12$, $p < 0.01$) and SO_4 ($r = 0.13$, $p < 0.01$) lagged 1 day, and with SO_2 lagged 2 days ($r = 0.11$, $p < 0.01$). Non-respiratory admissions showed no significant correlations during the summer. Asthma admissions were not significantly correlated to coefficient of haze, nitrogen dioxide, or humidity. **Although these findings are important this study did not address the times of year - spring and autumn - when asthma morbidity has been shown to rise. Associations between admissions and aeroallergens were not sought.**

Secondly, the study by Levy et al[33] compared pollution levels with weekly respiratory admissions (bronchitis, bronchiolitis, emphysema, pneumonia, and asthma) to 4 hospitals in Hamilton, Ontario from July 1970 till July 1971. Hamilton, with a population of 350,000 at the time, is a steel-producing city with significant industrial emissions. Pollutants were measured at a single station and included sulphur dioxide, coefficient of haze (COH)., oxidants, carbon monoxide, nitrogen oxides and hydrocarbons. As well an air pollution index (API) was computed from COH and

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• Coefficient of Haze is a measurement of particulate matter. Total particulate matter in $\mu g/m^3 = 75*(\text{COH units})^{1.14}$

sulphur dioxide levels.. Total weekly respiratory admissions had a highly significant correlation ($r=0.77$) with the API. Correlations became weaker for hospitals further away from the steel factory, and lost significance for the hospital furthest away. Significant correlations were also found between weekly respiratory admissions and monthly averages of SO_2 and COH. No correlations were found between admissions and carbon monoxide, oxidants, hydrocarbons, nitrogen dioxide, pollen, wind or humidity.

Thirdly, in Vancouver Bates et al[34] studied associations between emergency room visits at 9 hospitals and pollutants measured at 11 monitoring stations during the period of July, 1984 to June, 1985. Emergency visits were grouped into asthma, respiratory, and total visits. Visits were considered in 3 age groups: 1 to 14, 15 to 60, and 61 plus years. Asthma visits tended to vary by day of week with the highest day being Sunday. Pollutants, on the other hand showed little variation by day of the week. Pearson correlation coefficients were calculated between pollutants and deviations of visits from the mean visits for the same day of the week, the same year, and the same season. During the period of *May through October* asthma visits in all three age groups were significantly correlated with SO_4 ($r=0.16$ to 0.18, $p< 0.01$). Asthma visits in the 15 - 60 age group were also associated with SO_2 ($r= 0.12$, $p < 0.01$). During the period of *November through April*, asthma visits in the *61 and over age group only* showed associations with SO_2 ($r= 0.15$, $p < 0.001$) and SO_4 ($r= 0.18$,

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• $API= 2.5*(13.9*COH + 104.5*SO_2)^{0.8}$

$p < 0.01$). There were no associations between asthma visits and either ozone or NO_2 in either period. Associations between emergency visits and aeroallergens were not looked for in this study.

In follow-up to Bates' southern Ontario work, a study from New Jersey considered the effects of ozone on asthma[35]. Data was collected on emergency room visits for asthma as well as a comparison non-respiratory group of finger wounds in New Jersey between May and August in 1988 and 1989. These visits were compared with daily measurements of pollutants and meteorological factors. Analysis was done using multiple regression analysis. Asthma visits showed highly significant relationships with both ozone and temperature ($p<0.01$). Up to 15 percent of the variability of asthma admissions in this study could be explained by temperature and ozone levels.

In Los Angeles[28], daily emergency room visits to Childrens Hospital between August 1, 1979 and January 31, 1980 were compared with daily measurements of pollutants, weather and allergens (as has already been described). Pollutants were averaged from measurements at 5 stations and included coefficient of haze, hydrocarbons, NO, NO_2, O_3, and SO_2. Significant positive correlations that became strongest when pollutants were lagged 2 days were found for **coefficient of haze** ($r= 0.32$, $p < 0.01$), **hydrocarbons** ($r= 0.31$, $p < 0.01$), **NO** ($r= 0.41$, $p < 0.01$) and **NO_2** ($r= 0.22$, $p < 0.01$).

In Helsinki[36], asthma hospitalizations over a 3 year period were compared with pollutants and weather measurements. Data concerning daily asthma admissions was obtained from a register that documented all periods of illness that required hospitalization in Helsinki over the years 1987 - 1989. Pollutants which included NO_x, O_3, CO, and SO_2 were averaged from the measurements at a total of 4 sampling stations around the city. After adjusting for temperature, significant correlations were found between asthma admissions and same day measurements of SO_2 (r= 0.11, p =.001), NO (r= 0.17, p < 0.0001), NO_2 (r= 0.11, p=0.004) and O_3 (r= 0.11, p= 0.0008). The correlations with O_3 became stronger when this pollutant was lagged by one day (r= 0.16, p < 0.0001) or 2 days (r= 0.15, p= < 0.0001). Pollens and other aeroallergens were not considered in this study.

Weather: A number of ecological studies have looked for associations between weather and asthma admissions:

Firstly in Bates' southern Ontario study[32] (the methodological details of this study have already been described under pollutants) asthma admissions throughout southern Ontario were compared with temperature and relative humidity measurements. These weather variables were measured at a single central station located in London. Asthma hospital admissions in the winter were significantly correlated with temperature (r= 0.13 to 0.17, p < 0.001). However nonrespiratory admissions showed the same correlation. No association was found between asthma and relative humidity.

Beer et al[9] looked for associations of weather variables with asthma and other respiratory hospital admissions. They restricted their study to children 15 years and under who were admitted with acute respiratory illness to the emergency room of Assaf Harofeh Medical Centre, Israel during the period March 1, 1982 to May 6, 1985. Weather data was obtained from a meteorological station 3 miles from the hospital. They found significant correlations of biweekly asthma admissions with afternoon **gradients.** of **temperature** ($r= 0.36$, $p < 0.001$) and with afternoon gradients of the modified heat content factor (MHCF).. ($r= 0.51$, $p< 0.001$). No significant associations were found between asthma admissions and barometric pressure or humidity.

In the Los Angeles study[28] - which has already been described for allergens and pollutants - daily emergency room visits to Childrens Hospital were also compared with weather measurements between August 1, 1979 and January 31, 1980. The weather measurements were averaged from readings made at 3 monitoring stations in Los Angeles and included temperature, relative humidity, and wind speed. A negative correlation was found between asthma visits and **temperature** which was

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* Afternoon gradient = change in the variable between 2pm and 8 pm

** MHCF defined as the heat energy required to raise the temperature of water vapour to ambient levels.

strongest when temperature was lagged one day ($r = -0.24$, $p < 0.01$). **Wind speed** showed a positive correlation with asthma visits ($r=0.14$, $p < 0.05$).

In the study done in Helsinki[36] (methods have already been described under pollutants) daily asthma hospitalizations were compared with weather measurements as well as pollutants during the years 1987 -1989. Weather measurements were made at a single central station and included temperature, wind speed and relative humidity. Asthma hospitalizations showed a significant negative correlation with same day measurements of **temperature** ($r= -0.10$, $p=0.001$), and a positive correlation with **wind speed** ($r= 0.11$, $p= 0.03$). Relative humidity did not correlate with asthma admissions. Because wind is vital for the pollination of many plants[12] and because moving air plays a role in the dispersal of air pollutants[31], the association between wind and asthma admissions could be due to confounding.

Plausibility of these associations.

Thus O_3, SO_4, SO_2, NO_2, suspended particulate matter, temperature and wind speed have been associated with asthma hospital admissions. The plausibility of these associations has been shown through experimental studies:

Sulphur Dioxide: Linn[37] exposed 24 asthmatics to 0, 0.3 and 0.6 parts per million (ppm) SO_2 at separate sessions over a period of three weeks while they were exercising in a chamber for periods of 5 minutes. Significant increases in airway resistance (SRaw) and thoracic gas volume (Vtg) and significant decreases in airway conductance (SGaw) were found as SO_2 was increased. Similar results have been found by others[38].

Sulphates: Experiments on rabbits[39] have shown that high concentrations of sulphates impair mucociliary clearance in the airways. The specific effect on human asthmatics is not known.

Ozone: In 22 asthmatics, Linn et al[40] found that the combination of 0.2 ppm ozone and exercise in a sealed chamber for 2 hours did not significantly change FEV1 or forced vital capacity (FVC) compared with exposure to exercise alone. However, Folinsbee et al[41] have shown that a cumulative effect of higher doses of ozone may be important. In healthy volunteers who were exposed to 0.35 ppm and 0.55 ppm ozone for 2 hours daily, significant airway obstruction developed after 3 days. Lower levels of 0.2 ppm repeated up to 5 days had no effect.

Nitrogen Dioxide: Studying 15 asthmatics, Bauer[42] found that exposure to both 0.3 ppm NO_2 via mask and exercise reduced forced expiratory volume in one second (FEV1) significantly more than exposure to either exercise or NO_2 alone. In 13 of 20 asthmatics that Orehek[43] studied, exposure to 0.1 ppm NO_2 in a sealed room for one hour significantly increased airway resistance and non-specific airway reactivity compared to exposure to air.

Temperature: Cooler temperatures appear to exacerbate asthma. This was shown by Linn et al[37] who exposed 24 asthmatics to purified air in a chamber while exercising at temperatures of 21, 7 and minus 6 degrees celsius. Airway resistance increased significantly at lower temperatures.

Wind: While wind itself probably doesn't exacerbate asthma it is important in the dispersal of other factors that do such as pollen[11] and pollutants[30].

Summary of confounders.

Therefore temperature, wind speed, as well as O_3, SO_2,SO_4, and NO_2 and particulate matter have previously been associated with asthma admissions and may also be related to pollen levels. As described in Figure 1a, these factors may be confounders and should be considered when looking for an association between pollen and asthma admissions during the spring.

EFFECT MODIFICATION.

It has already been described how pollen can enhance bronchial responsiveness to other factors[19]. It may therefore be possible for pollen to modify the effect that other environmental factors have on asthma hospitalizations. A proposed mechanism for this is presented in Figure 1 b. Basically, exposure to high pollen levels may increase the sensitivity of asthmatics to other environmental factors. Thus asthma exacerbation and subsequent hospitalization may be more likely after exposure to an environmental factor (such as O_3) when pollen levels are high, than when they are low. Potentially then this could present as an increase in correlations between asthma hospitalizations and an environmental factor (such as O_3) when pollen levels are high. This question has not been addressed by other ecological studies and is worth considering in this study.

SUMMARY

In Ontario - and in other countries - hospital admissions for asthma increase during the spring and again during the autumn. The spring-time increase coincides with the pollen season of trees and grasses. Pollen grain allergens can exacerbate asthma and have even been related to asthma hospital admissions in New Orleans. However their association with asthma admissions during the important spring season remains unproven.

Some pollutant and weather factors are known to exacerbate asthma and some - O_3, SO_2, SO_4, particulate matter, wind speed and temperature -have previously been associated with asthma admissions. The effect that high pollen levels have on associations between these factors and asthma needs to be considered (ie possible

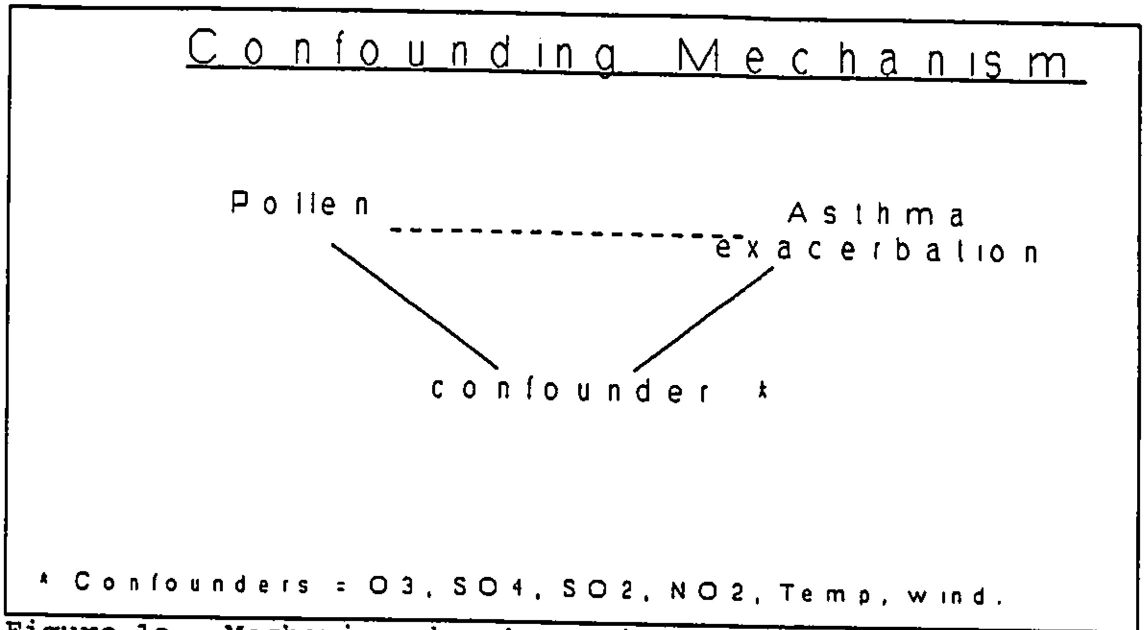


Figure 1a. Mechanism whereby environmental variables may act as confounders between pollen and asthma.

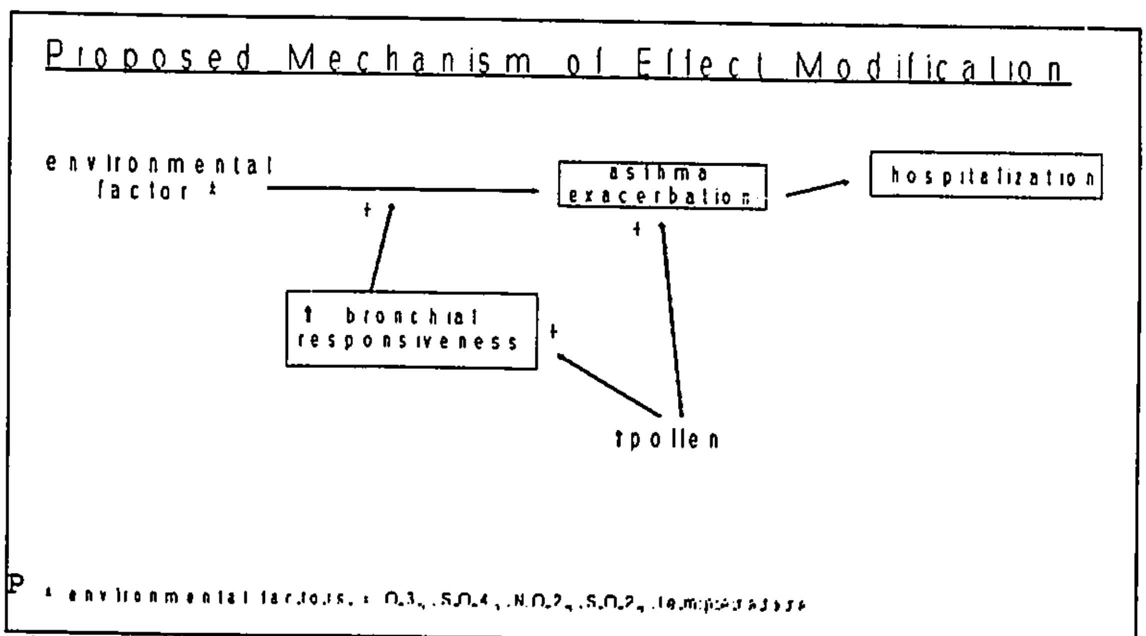


Figure 1b. Proposed mechanism whereby pollen may modify the effect that other environmental variables have on asthma admissions.

effect modification). Moreover, many of these environmental factors may be related to both pollen levels and to asthma and they therefore need to be ruled out as confounders.

OBJECTIVE:

To determine if asthma hospital admissions during the spring are related to levels of airborne pollens in Southern Ontario.

HYPOTHESES:

(1) Daily asthma emergency room (E.R.) admissions between March and July are significantly associated with daily grass, tree and total pollen counts. These associations are stronger when pollen is lagged by one or two days.

(2) Weekly asthma E.R. admissions between March and July are significantly associated with grass, tree and total pollen counts from the same week.

(3) Weekly averages of ozone, sulphate and temperature measurements between March and July will show associations with weekly asthma admissions which are larger when pollen counts are elevated.

RELEVANCE OF TOPIC:

Although the presence of a spring peak in asthma morbidity has been documented, the cause of the peak has not been established. Other studies have looked at associations between asthma morbidity and environmental variables but have not concentrated on the spring season increase in morbidity. Definition of factors which are associated with the spring peak is required.

Strong associations may point to further research which may confirm causal associations and have implications for prevention. For example, if a particular allergenic pollen is strongly related to springtime asthma morbidity, sensitive asthmatics could be monitored more closely and receive higher doses of medication during the brief pollen season.

B. METHODS:

STUDY DESIGN:

This study was ecological in design. Asthma emergency room admissions - defined as admissions to the hospital through the emergency room (E.R.) - were compared with measurements of pollens, pollutants and meteorological variables on daily and weekly bases. The study analyzed data that was already available as described below (under the heading Data Sets).

REFERENCE POPULATION:

The reference population were those living in London and St. Thomas, Ontario during the years 1983-1988. The population of this area was approximately 370,000 during the 1986 census. The area is surrounded by rich agricultural land. The McDonald Cartier Freeway (Highway 401) separates London in the north from St. Thomas in the south[44,45].

STUDY PERIOD:

The study was restricted to 1983-1988, the years for which complete data was available for all data sets. The months of study were March to July for each of the years. These months were chosen as they contain the full tree and grass pollen seasons and allow a month on either side of the expected spring increase in asthma morbidity.

DATA SETS:

Emergency Hospital Admissions: This data was obtained for Southern Ontario from the Ontario Ministry of Health Hospital Morbidity Files. The data includes all admissions to the hospital through the emergency room during the years 1983-1988. Emergency admissions for asthma (ICD-9 code 493) were extracted from this file. Also extracted was a comparison group of medical, non-respiratory emergency admissions. This latter group included subarachnoid haemorrhage, gastric and duodenal disorders, pancreatic disorders, and pyelonephritis, (ICD codes 430, 530-537, 577, and 590-592). Each record contains admission date, birth date, sex, residence code, hospital code, and diagnostic code.

Only individuals who were resident in the London, St. Thomas or areas in between (residence codes 401-402, 1900-1903) were included in the analysis. The analysis was further restricted to those admitted to one of the 4 hospitals in the area: St. Josephs Hospital, University Hospital, Victoria Hospital, and St. Thomas Elgin General Hospital. These restrictions by hospital and residence were necessary to improve the likelihood that an individual admission was exposed to the environmental variables as measured.

Admissions were aggregated by date. Therefore the unit of observation was the daily or weekly number of asthma admissions for a defined age range in London - St. Thomas.

Because the admissions data are based on hospital separations, one individual could contribute more than one admission over the study period.

Pollen Counts: Allergist Dr. John Toogood provided daily pollen counts for London, Ontario for the years 1965-1991. The counts were collected on a Durham Gravitational Sampler® which, since the early 1960s, has been placed on top of the Victoria Hospital in London, eight storeys up. The pollen counts on the sampler slides have been read by the same individual since the 1960s. Data is reported as grains per square centimetre (gn/cm^2) of slide surface for each day. For weekly analyses the daily values were summed to obtain a total for the week. **Counts were available for total trees, and total grasses. No individual species pollen counts were available.** Complete fungal spore data was not available.

Durham gravitational samplers are known to be affected by wind[46,47,11]. The amount of pollen settling on the Durham slides will vary depending on wind speed and direction[12]. It is not possible to adjust for the affects of wind on the samplers because wind speed and direction are constantly varying throughout the course of a day. Therefore the pollen counts are at best *semi-quantitative.*

Because of this semi-quantitative nature of the pollen data, *pollen counts were treated categorically* by dividing them into one of four groups (ie low, medium, high or very high). The cutpoints used to determine which group a pollen count fell into were based on *quartiles.* Therefore approximately 25 percent of the days over the full study period had pollen counts that were in the lowest quartile, 25 percent in the highest category, and 25 percent in each of the two middle categories. It is not known precisely how semi-quantitative pollen levels relate to clinical asthma morbidity. Therefore the biological significance of these cutpoints cannot be determined.

Meteorological data: Daily data was obtained from Environment Canada for London Airport for the years 1981- 1990. The variables used in this study on a daily basis included mean temperature, maximum wind speed, maximum relative humidity, precipitation, and maximum barometric pressure. On a weekly basis the mean values were computed from daily measurements of maximum wind speed, minimum temperature, maximum relative humidity, precipitation and maximum barometric pressure for during the week.

Ambient Air Pollution: Pollutant data was provided by the Ontario Ministry of Environment for Fairgrounds Station in central London for the years 1983-1988. The data included daily means for SO_4, and NO_3 and daily maximums for SO_2, NO_2, and O_3. Standard and reliable methods were used for measuring the pollutants by the Ontario Ministry of Environment: SO_4 and NO_3 were collected on glass fibre filters by high volume samplers and subsequently extracted by digestion in distilled water. They were measured colorimetrically[31] and the measurement has been reported in micrograms per cubic meter (ug/m^3). The measurement of O_3 and NO_2 were based on the principle of chemiluminescence[31] and they were reported in parts per billion (ppb). SO_2 was measured by fluorescent excitation[31] with pulsed ultra-violet radiation and was also reported in ppb. **Data for particulate matter was not available.**

All of the above databases were linked to form a master database sorted by date.

ANALYSIS:

Overall Analytic Approach: In this study, time series data of a large number of variables were analyzed. The goal was to determine if changes in the dependent time series variable (asthma admissions) could be explained by changes in the other time series (pollen, pollutants and weather). The most straight-forward method for comparing such series is ordinary least squares (OLS). With OLS methods, values of one time series at a given point in time are cross-correlated with values of another series at the same point in time.

A number of potential biases have been described which may affect the analysis of such time series data[48]. Firstly, secular trends in one or more of the variables may be present and should be removed in order to obtain stationarity. Such trends may be present for reasons other than a causal relationship between the variables being considered. If this is the case, a spurious correlation may be found between two variables that show similar secular trends. Secondly, seasonal trends may be present in the data. Seasonality may bias results in a way similar to secular trends, and thus should also be removed from the data prior to analysis. Thirdly, autocorrelation and autocorrelated errors may play a role. Values in each of the time series may be serially dependent (ie values at one point in time may be dependent upon previous values). Such autocorrelation in a variable is part of that variables own orderly behaviour and should not be predicted by a second variable.

In order to deal with such biases, autoregressive integrated moving averages (ARIMA) has been suggested as a preferred method of analysis for time series data. A first step in ARIMA, prior to cross-correlating two time series, is to remove underlying trends and autocorrelations. Essentially each series is adjusted for its own pattern of autocorrelation thus producing a transformed series. It is these transformed series, with the underlying biases removed, that are then cross-correlated with one another.

Although ARIMA may be a *choice* technique for analyzing time series data, it was not attempted in this study for three reasons. Firstly, multivariate ARIMA is a very advanced technique which requires adequate training in order to obtain reliable results. Repeated attempts are required to identify ARIMA models - a process which has been described as an art on the analyst's part. While OLS methods may be more open to bias, it is of interest to note that of the numerous previous ecological studies dealing with asthma hospitalizations and environmental factors, all used OLS methods and none attempted ARIMA. This suggests that OLS methods are still acceptable in the published literature in this field. Secondly, the pollen data used in this study can only be considered as semi-quantitative. It was necessary to treat this data categorically for multivariate analyses. This data would therefore be unsuitable for a multivariate ARIMA. Finally, an attempt was made to adjust for biases due to trends and seasonality using other methods described below. Therefore least squares methods and nonparametric methods have been used for analyses in this study following these adjustments.

Restriction by Season: To reduce the effects of seasonality, the study was restricted (as already described) to the months of March through July in each of the study years.

Adjustment for weekday and annual trends: Asthma hospital admissions have shown both an increasing annual trend and variation by day of the week in previous studies[34]. A method that has been described by Bates[32] to adjust for these trends basically compares admissions on a given day with all of the same weekdays during the same year. To do this, analyses were based on observed to expected ratios. For daily analyses the admissions were expressed as the ratio:

$$\frac{\text{actual number of admissions on a given day}}{\text{mean number of admissions that occurred on all of the same weekdays during the March-July period of the same year.}}$$

For weekly analyses admissions were expressed as the ratio:

$$\frac{\text{actual number of admissions during a given week}}{\text{mean number of admissions that occurred for all weeks during the March-July period of the same year.}}$$

This method should remove the affect of variation by day of the week, and also adjust for underlying year to year changes in admissions.

Because a ratio is used to adjust for the trends the resulting distribution may be asymmetrical with values ranging from zero to one when the numerator is less than the denominator, and values ranging from one to infinity if the numerator is greater than the denominator. However the denominator in these ratios is the mean value of all values of the numerator. In this study weekly admissions did not exceed twice the mean weekly admissions. Therefore the ratio would show a range of zero to one for weeks with admissions less than the mean and one to two for weeks with admissions greater than the mean. Furthermore, non-parametric methods were used in this study for analyses on a daily and weekly basis. The ranks assigned in non-parametric methods would be unaffected by any asymmetry in the resulting distribution.

Descriptive Analysis: To characterize the raw data and demonstrate peaks and trends in admissions over the study years (1983-1988), emergency asthma admissions were plotted against time with number of admissions on the Y-axis and date on the X-axis. Similarly, pollen and other environmental variables were plotted against time. Annual means were computed to look for long term trends.

To better demonstrate the seasonal pattern of asthma admissions, monthly deviations from a 12 month moving average were computed. This would essentially *remove the underlying year to year trend* therefore making it acceptable to average the monthly values over the six year study period. These averaged values were then used to produce a plot of the *average percent variation about the trend.*

Correlation: Spearman rank correlation were used to look for associations between admissions, pollen and other environmental variables. For weekly analyses, asthma admissions were stratified into three age groups (less than 5, 5 to 34, and 35 plus years). For these analyses, pollen was treated as a continuous variable.

Analysis of Variance: Associations between admissions and pollen counts were also sought using Analysis of Variance (ANOVA). Pollen counts were categorized into four groups (ie low, medium, high or very high) based on quartile cutpoints. *ANOVA* was used to test if the mean number of admissions were significantly different between the 4 groups. Because the assumption of normality may not hold up (particularly on a daily basis) the non-parametric *Kruskall-Wallis test* was also used to test if the median number of asthma admissions were significantly different between the 4 groups.

Linear contrast was used to look for a *positive tendency* of admissions to increase going from the lowest to highest pollen quartiles. It is possible that higher levels of interaction - such as a quadratic relationship - might exist between pollen and asthma admissions. However because of the semi-quantitative nature of the pollen counts in this study it would likely not be possible or worthwhile to determine such an exact relationship.

Control of Confounders: Analysis of Covariance was used to control for the effects of pollutants and weather variables that may have confounded the association between pollen and asthma admissions.

Stratification: To determine if elevated pollen increased the association of asthma admissions with weather or pollutants, stratification by pollen count was done (greater and lower than median). Spearman correlations between asthma and pollutants and weather were then repeated for the two strata.

Daily and Weekly Analyses: Analyses were done on both daily and weekly bases in this study. Daily analyses allowed consideration of a several day lag effect that may be present between exposure and outcome. Weekly analyses were done to confirm associations that were found on a daily basis. As well, a weekly basis was used for multivariate analysis (ANCOVA) because expected daily admission numbers were small and therefore had a very high variance.

DETECTABLE SIZE OF CORRELATIONS:

Table I shows critical values for Spearman correlations. Based on a total of 138 weekly observations over the study period (March-July for 6 years), a correlation of between 0.159 and 0.174 could attain significance at the 5 percent level. For daily analyses, with a total of 904 observations, a correlation of just over 0.062 is required to achieve significance at the 5 percent level.

Table I Values of rank correlation coefficient required to achieve statistical significance for various levels of significance and observation sizes.

	Number of Observations			
significance level	125	150	500	1000
0.05	.174	.159	.088	.062
0.01	.228	.208	.115	.081

C. RESULTS

ADMISSIONS:

There were a total of 1163 admissions to hospital through the emergency room at the 4 hospitals during the months of March through July over the six year study period. The mean age of patients at admission was 26.3 years with a range of 0 to 98 years. Males made up 49.8% of the total admissions. Because the expected number of daily admissions was small - zero on a large number of days -the frequency distribution of daily admissions is a poor approximation of normal. Weekly admissions follow an approximately normal distribution.

Table II shows the mean number of emergency asthma admissions by day of the week during the study period. There was a significant difference in the mean number of admissions by weekday. The highest number of admissions were on Mondays and Tuesdays, while the fewest admissions tended to occur on weekends.

Table II: Mean Number of Asthma Admissions by Day of Week

Mean Number of Admissions							ANOVA p
Mon	Tues	Wed	Thur	Fri	Sat	Sun	
1.49	1.42	1.22	1.19	1.36	1.03	1.16	0.01

ANNUAL TENDENCY:

Emergency Asthma Admissions. Figure 2 shows monthly E.R. asthma admissions from 1983 to 1988. Many peaks in admissions occurred throughout the study period. The number of monthly admissions appears to have shown some increase during the 6 years.

Pollen, Weather and Pollutants. Table III shows the annual means of daily values of meteorological variables, pollutants and pollens for each of the six years. None of the variables demonstrates a consistent rising or falling trend over the six year period.

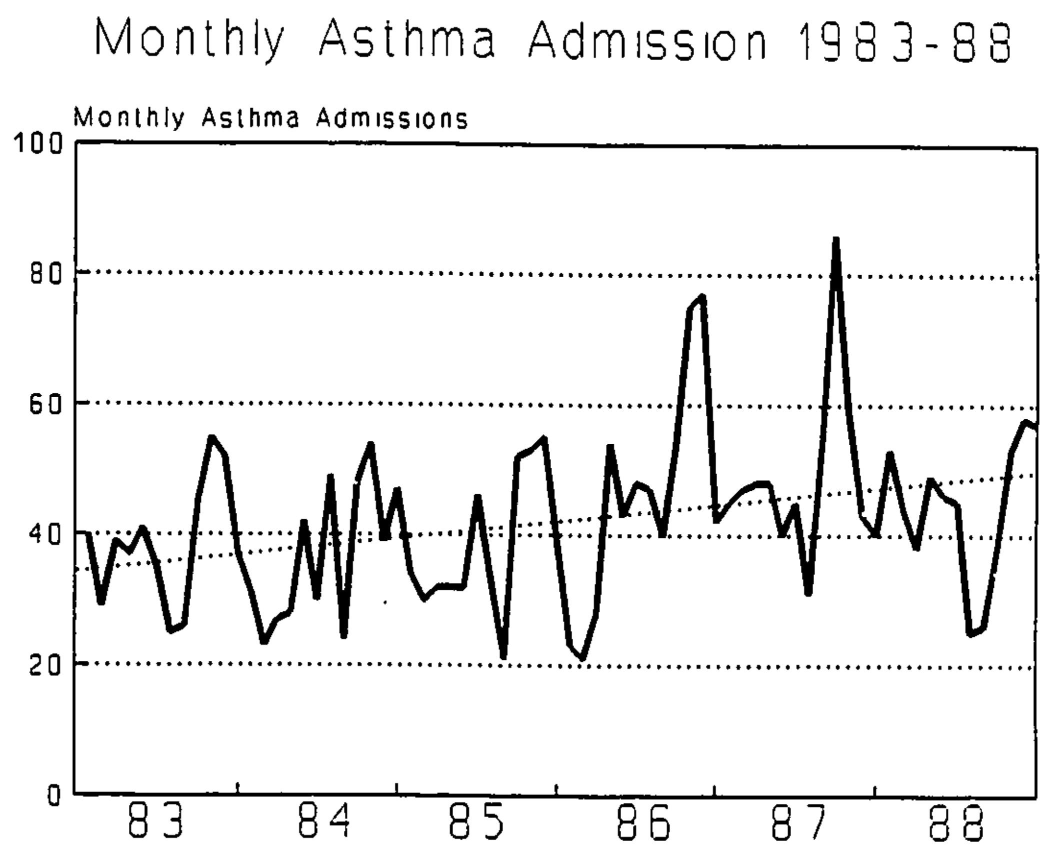


Figure 2 TREND IN MONTHLY ASTHMA ADMISSIONS IN LONDON, ONTARIO 1983-1988.

Table III ANNUAL MEANS OF DAILY ENVIRONMENTAL VARIABLE MEASUREMENTS

	83	84	85	86	87	88
Mn Win Sp	15.58	14.73	15.24	14.21	13.35	13.51
Mn Wind Dir	218.27	204.52	211.31	213.59	202.95	219.6
Max Baro Pr kp	98.3712	98.4588	98.4742	98.5095	98.5655	98.4818
Min Baro Pr kp	97.8163	97.8084	97.8004	97.8825	98.0494	97.9203
Max Temp C	16.827	15.541	17.659	17.637	19.552	18.324
Min Temp C	6.066	5.289	6.274	6.783	7.935	6.241
Max Hum %	91.17	88.09	91.07	88.88	89.35	83.59
Min Hum %	52.72	53.06	48.13	53.59	47.97	45.6
Precip mm	37.63	37.96	28.39	32.15	21.08	23.69
Trees gn	15.15	43.52	23.07	22.24	26.59	31.27
Grasses "	5.32	3.87	3.11	3.16	2.79	3.25
SO4	5.85	4.47	4.82	5.57	6.4	5.99
NO3	3.89	3.89	4.74	4.7	5.16	4.48
SO2 Max	9.8	9.17	6.47	8.14	9.07	8.1
NO2 Max	37.08	40.75	43.66	43.84	42.6	36.69
O3 Max	47.21	44.39	47.13	44.39	48.48	51.77

DESCRIPTIVE PLOTS:

To help characterize the data, the following descriptive plots of the variables are provided:

Emergency Asthma Admissions. Figure 3 shows daily asthma admissions averaged by month for each of the years 1983 - 1988. While these have not been tested statistically for seasonality, there appear to be two or more periods of increased admissions in each of the six years. The most admissions tended to occur each autumn generally between September and November. There also appeared to be some increase in admissions during the spring months (April, May and/or June) of at least some of the years when compared with the surrounding months. The fewest number of asthma admissions occurred in August of each year, with the exception of 1987 when July had the fewest.

In order to further summarize the emergency asthma admission data monthly deviations from 12 month moving averages have been calculated. Because this removes the underlying year to year trend, it is acceptable to average these monthly values for the six study years obtain an average percent variation about the trend. Figure 4 shows the six year average percent variation about the trend for asthma emergency hospital admissions in London-St.Thomas. Admissions appear to have increased during two seasons over the study years: a small increase during April-June and a larger one extending from September-November.

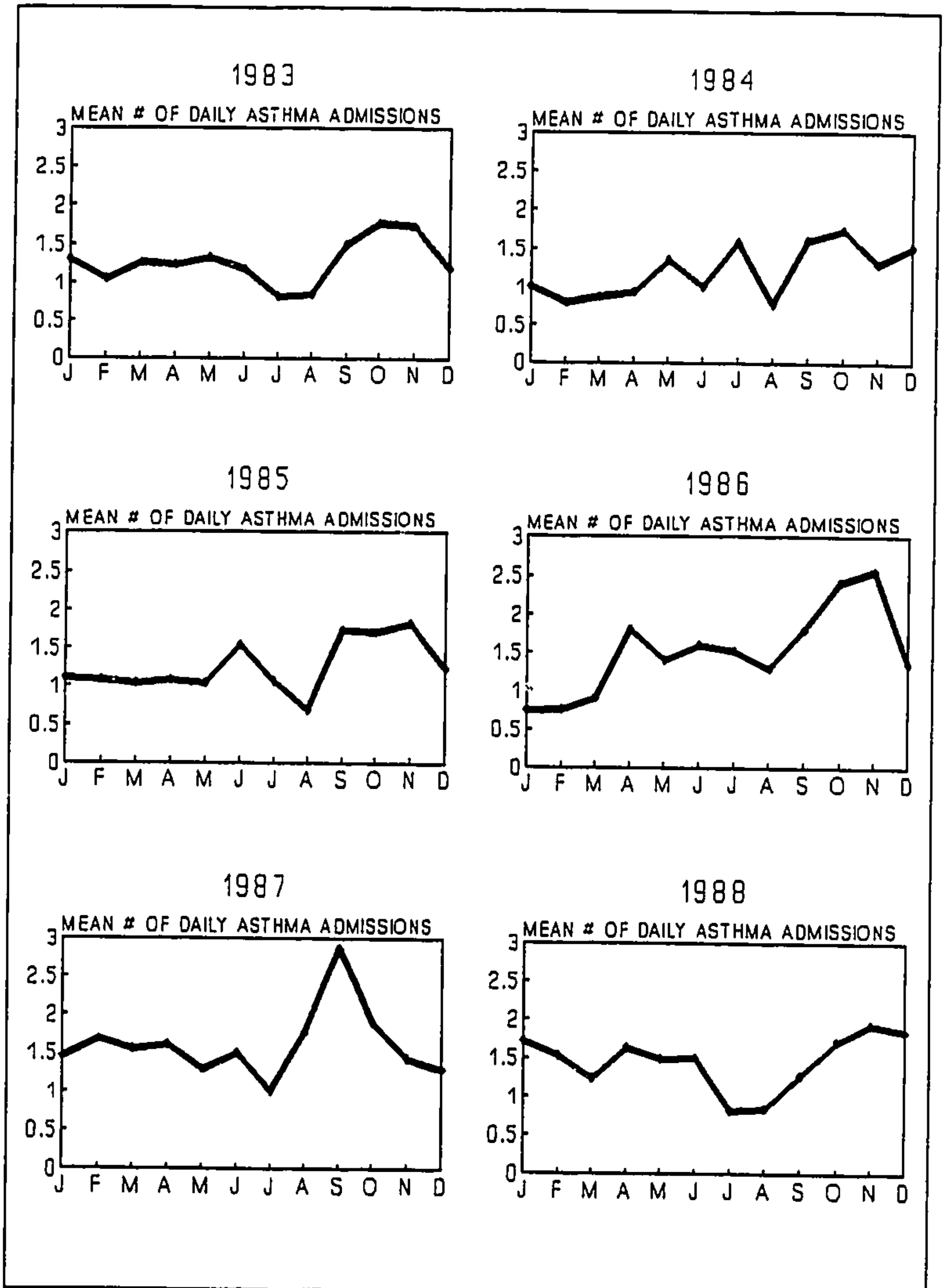


Figure 3 Monthly Means of Daily Asthma Admissions 1983-1988

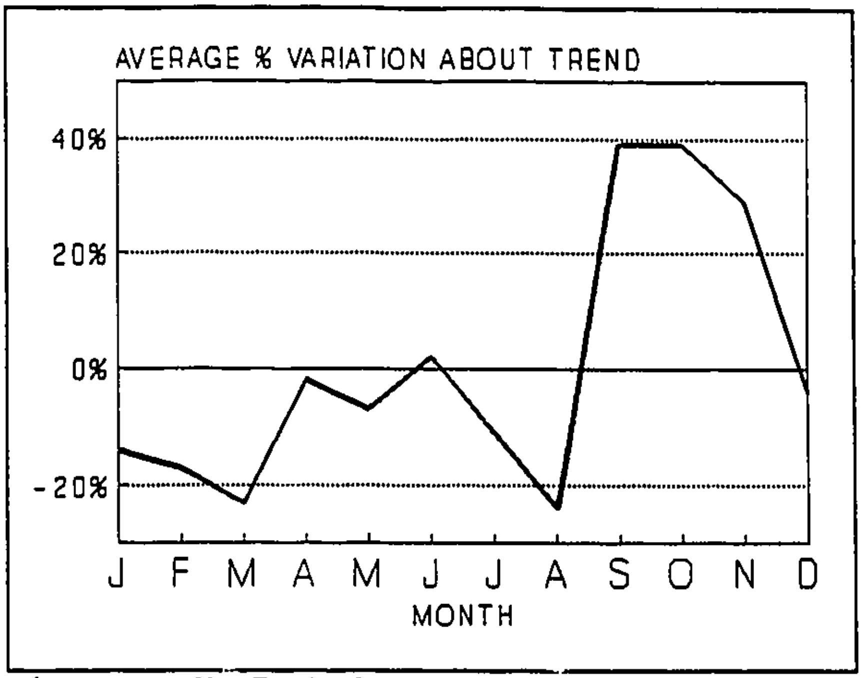


Figure 4 MONTHLY ASTHMA ADMISSSIONS AVERAGE PERCENT VARIATION ABOUT TREND 1983-88 FOR LONDON, ONTARIO.

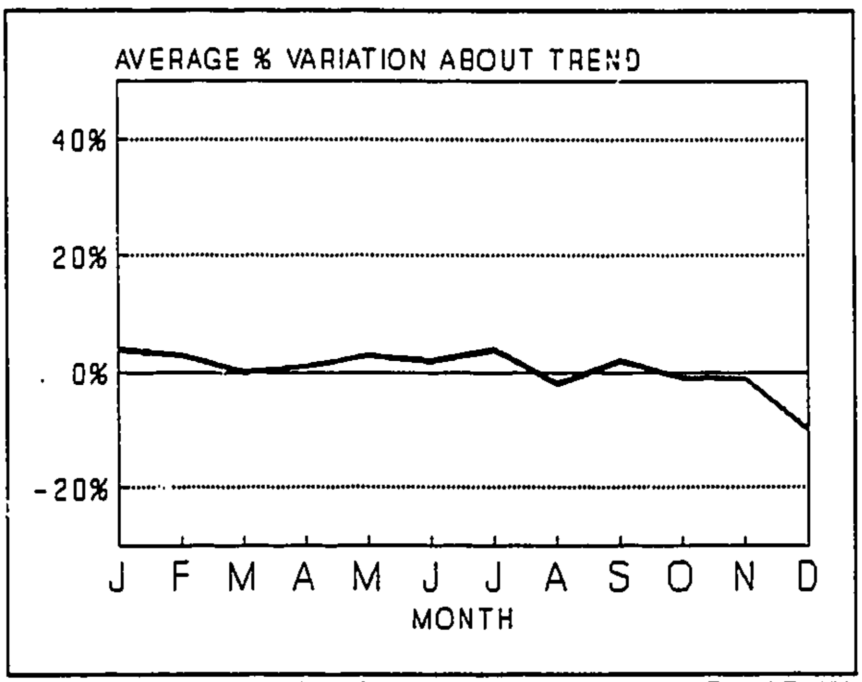


FIGURE 5 MONTHLY NON-RESPIRATORY ADMISSSIONS AVERAGE PERCENT VARIATION ABOUT TREND 1983-88 FOR LONDON, ONTARIO.

Non-respiratory admissions. Figure 5 shows the six year average percent variation about the trend for non-respiratory emergency hospital admissions in London-St.Thomas. Although there was some increase in admissions in the spring and early summer, and a drop during August, the amount of seasonal variation was considerably less.

Pollen. Figures 6 and 7 show the monthly means of respectively daily tree pollen counts and daily grass pollen counts during each of the six study years. Monthly means of daily asthma admissions are also shown in each plot for comparison. A peak in the measured total tree pollen occurred each year in April or May. Grass pollen counts were considerably lower than total tree pollen counts. A peak in the grass pollen occurred in June of each year.

Pollutants. Figures 8-13 show monthly means of daily values for 5 pollutants - O_3, SO_2, NO_2, SO_4, NO_3, - for each of the six study years. Monthly means of daily emergency asthma admissions for the same year are also shown for comparison in each figure. NO_2 showed springtime increases during April, May or June in 5 of the years (1983 and 1985 - 1988). SO_2 tended to be highest in the winter and fall during the spring whereas ozone and SO_4 typically rose through the spring months to peak in the summer.

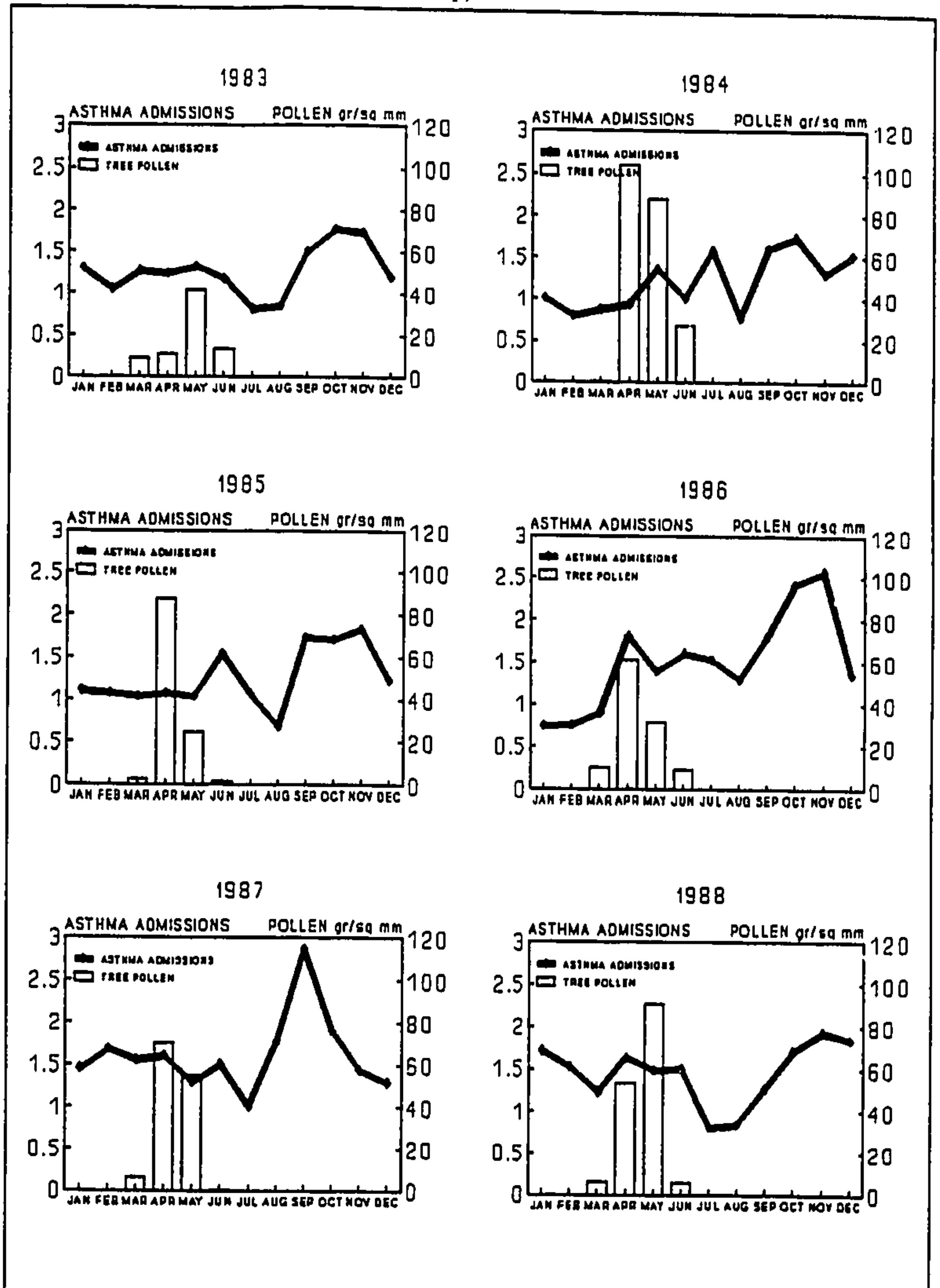


Figure 6. Monthly Means of Daily Asthma Admissions and Monthly Means of Daily Tree Pollen Measurements

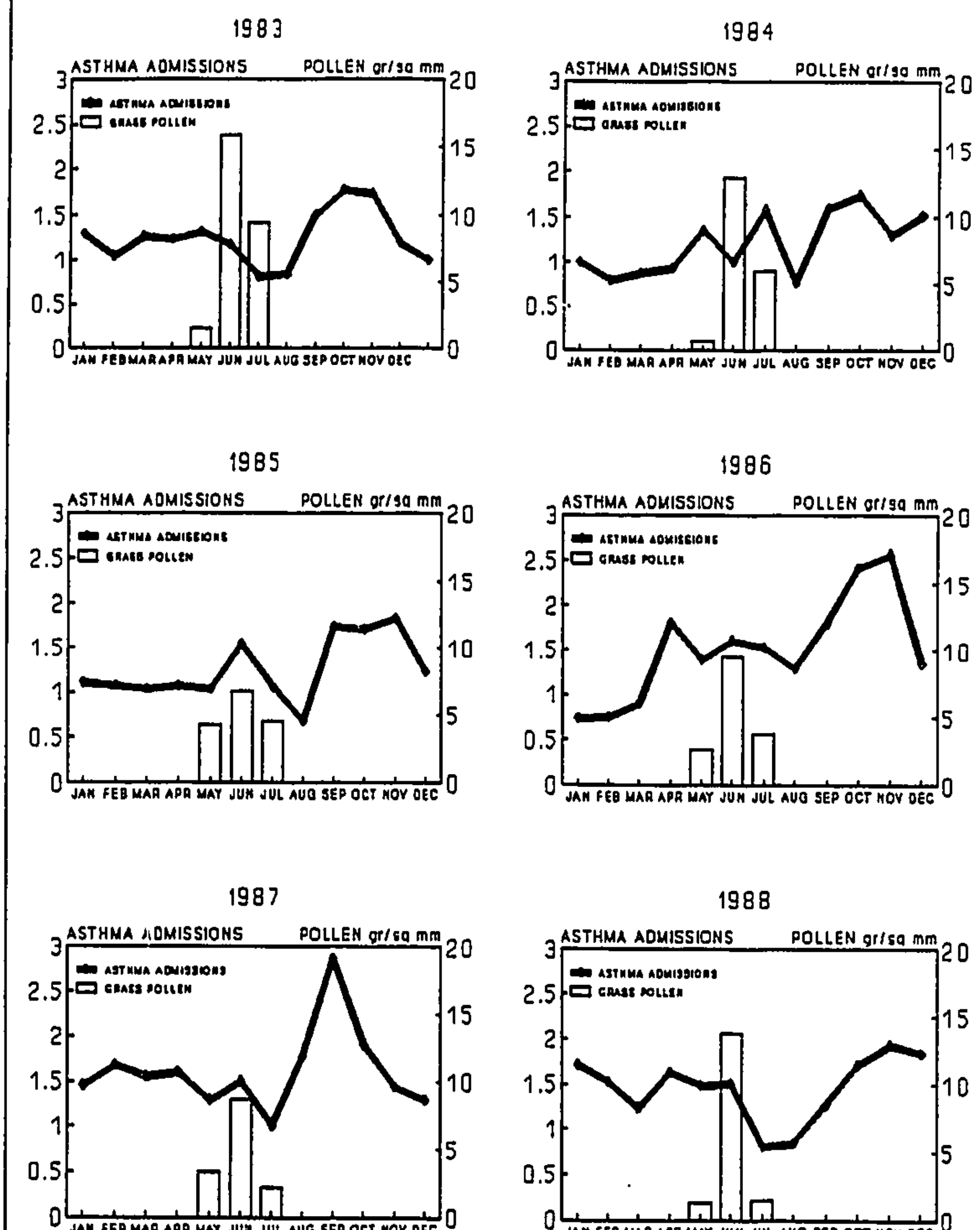


Figure 7. Monthly Means of Daily Asthma Admissions and Monthly Means of Daily Grass Pollen Measurements

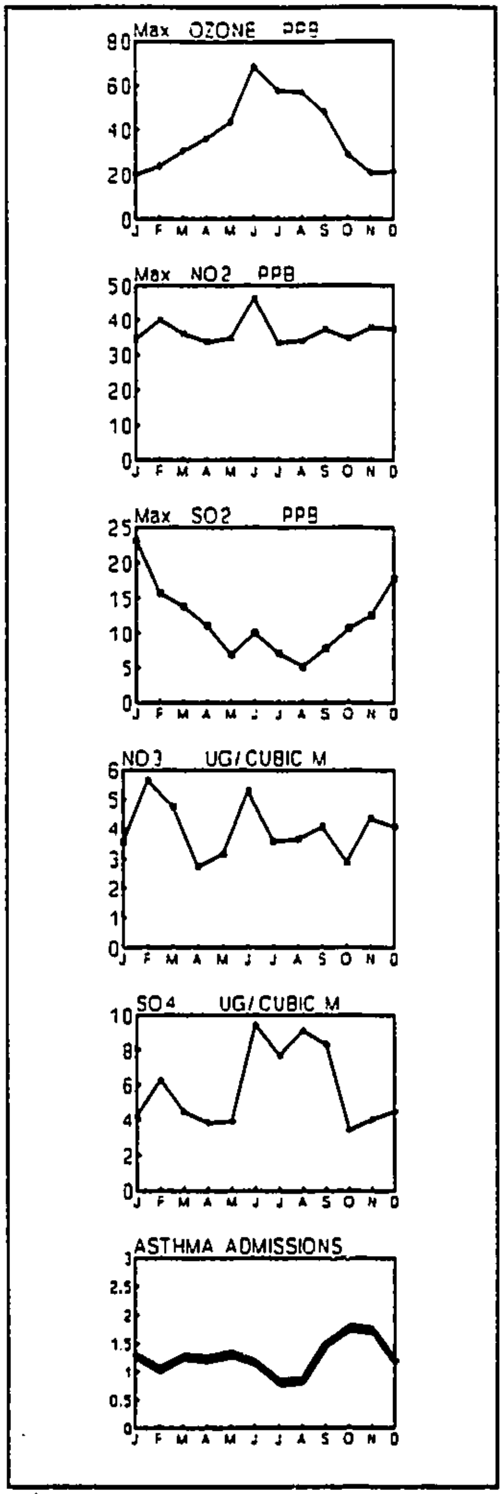


Figure 8. 1983 Monthly Means of Daily Asthma Admissions and Daily Pollution Measurements

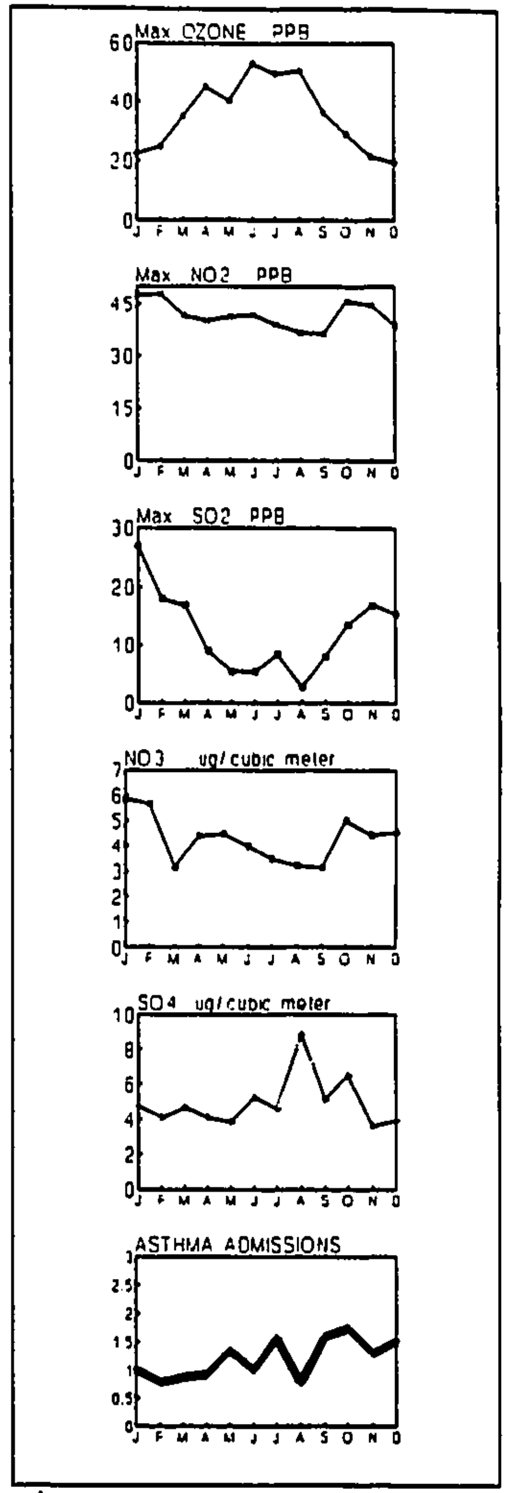


Figure 9. 1984 Monthly Means of Daily Asthma Admissions and Daily Pollution Measurements

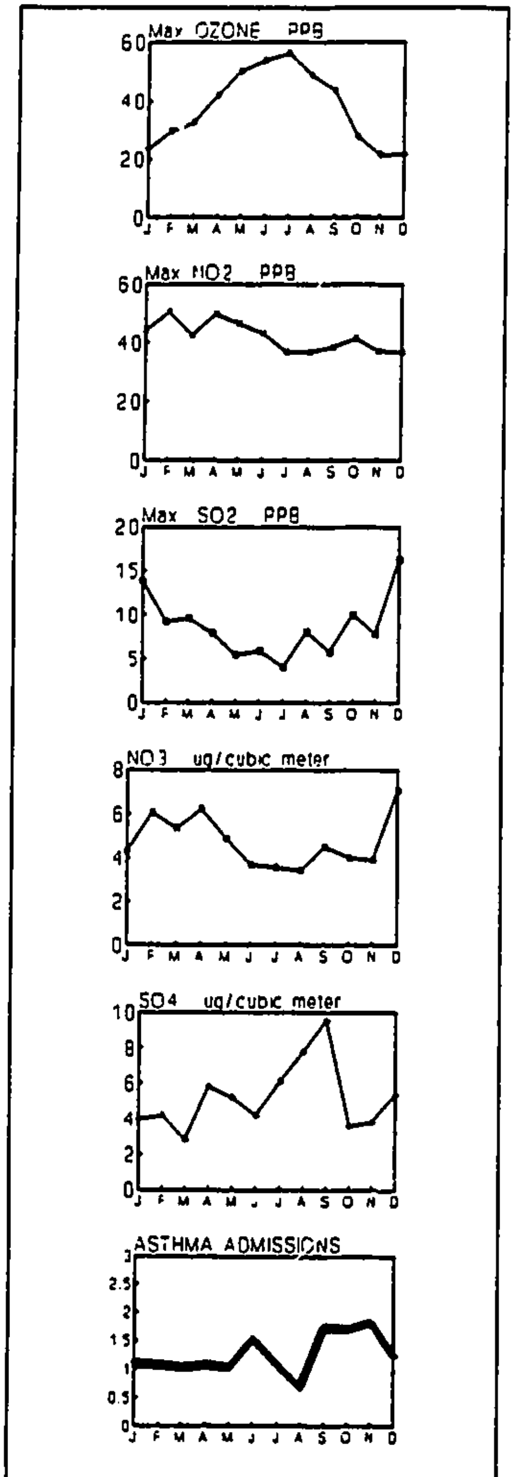


Figure 10. 1985 Monthly Means of Daily Asthma Admissions and Daily Pollution Measurements

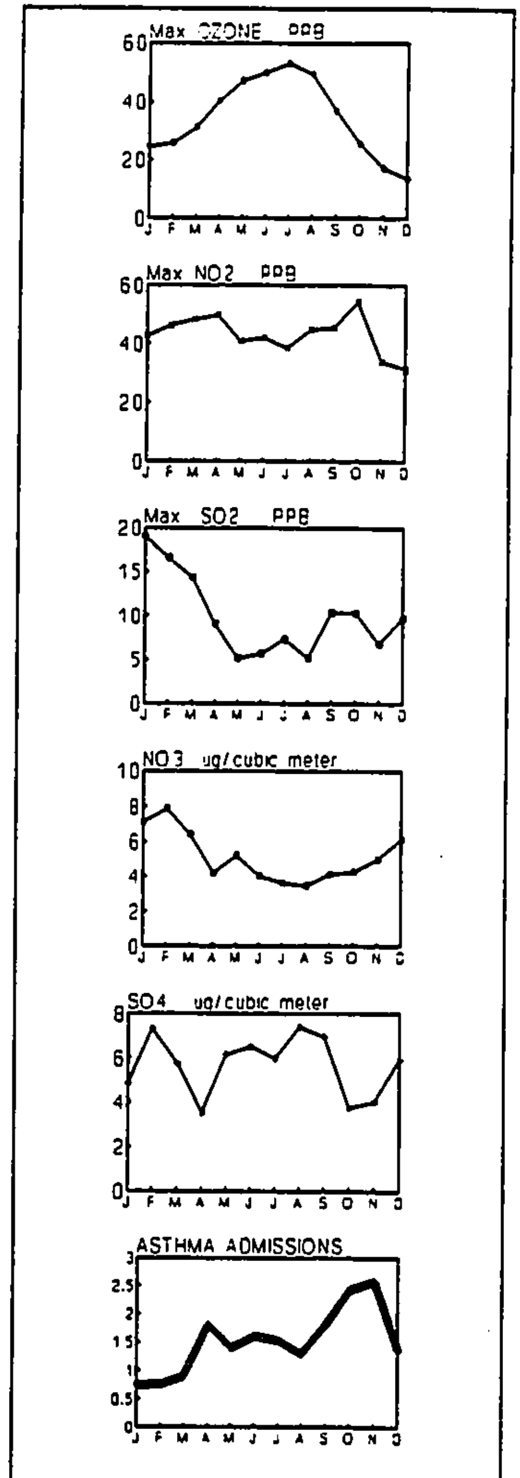


Figure 11. 1986 Monthly Means of Daily Asthma Admissions and Daily Pollution Measurements

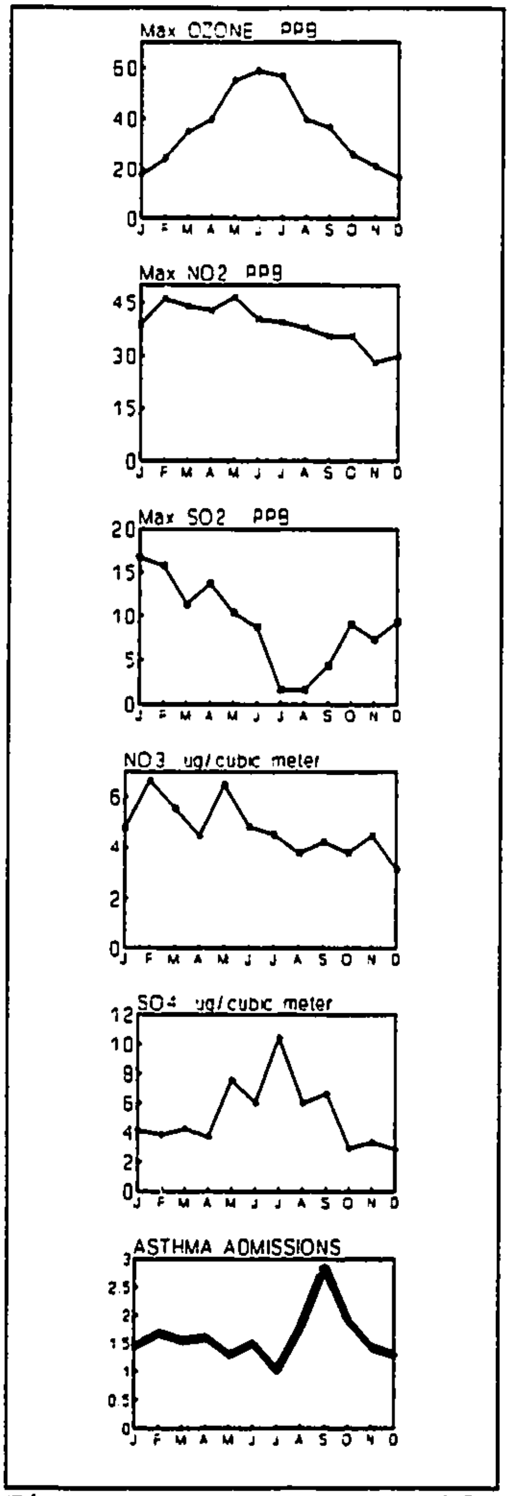


Figure 12. 1987 Monthly Means of Daily Asthma Admissions and Daily Pollution Measurements

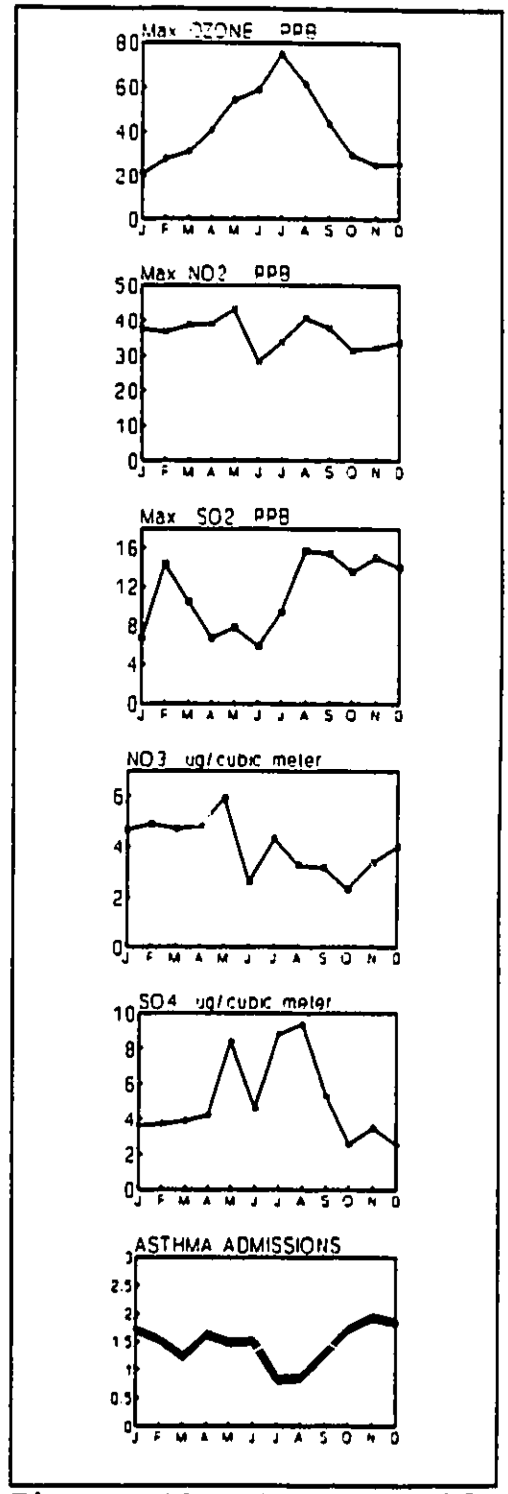


Figure 13. 1988 Monthly Means of Daily Asthma Admissions and Daily Pollution Measurements

Weather. Figures 14-19 show monthly averages of daily measurements of 5 meteorological variables - precipitation, maximum relative humidity, temperature, barometric pressure, and maximum wind speed - for each of the six study years. Monthly means of daily emergency asthma admissions for the same year are also shown at the bottom of each plot for comparison. Temperature rose during the spring and peaked in July and August each year. Precipitation showed no consistent seasonal pattern. Maximum relative humidity tended to rise from a low in the winter and spring to a high in the summer and autumn. Barometric pressure was generally lowest in April or May and rose during the autumn and winter months. Wind speeds were generally highest in the winter and lowest during the summer months.

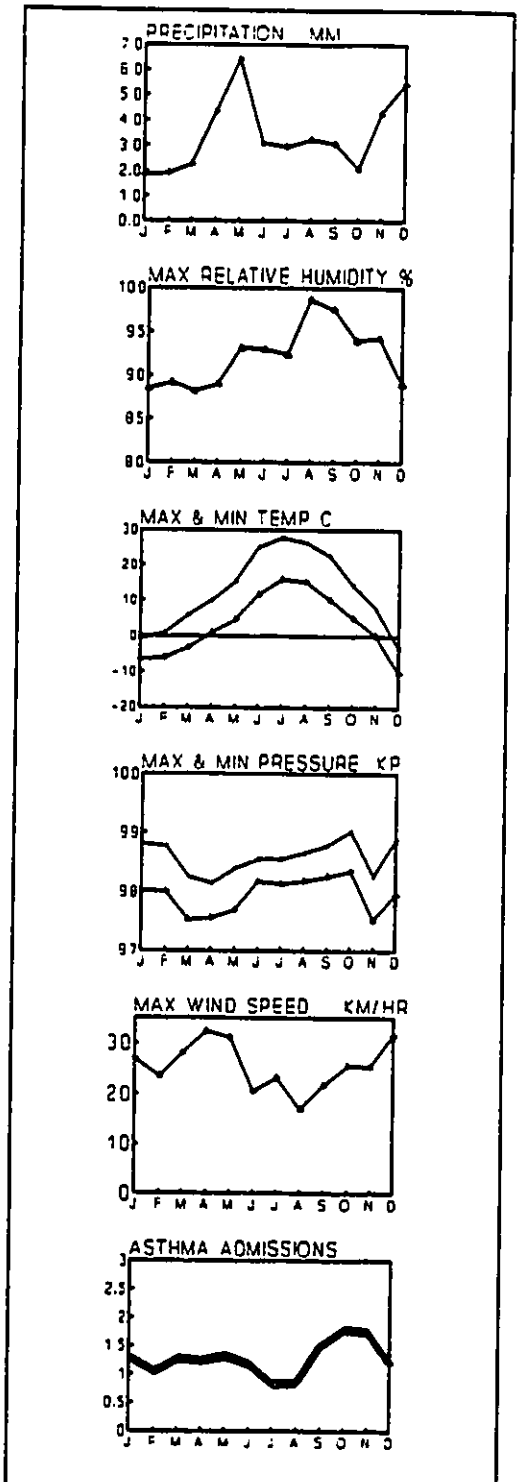


Figure 14. 1983 Monthly Means of Daily Asthma Admissions and Daily Weather Measurements

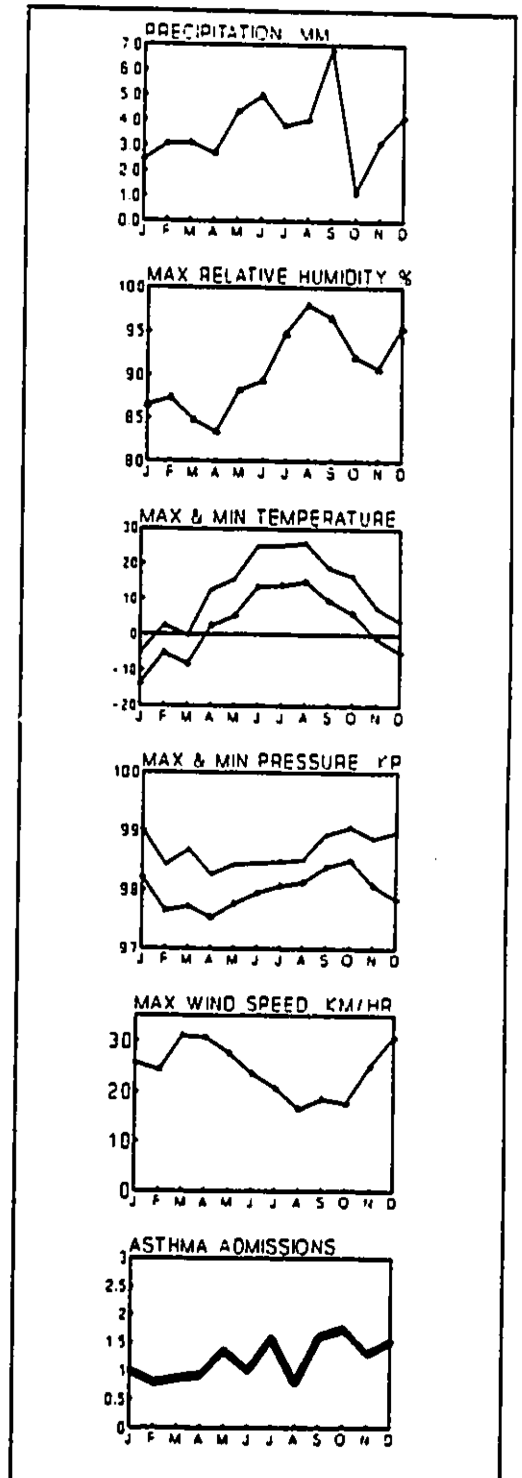


Figure 15. 1984 Monthly Means of Daily Asthma Admissions and Daily Weather Measurements

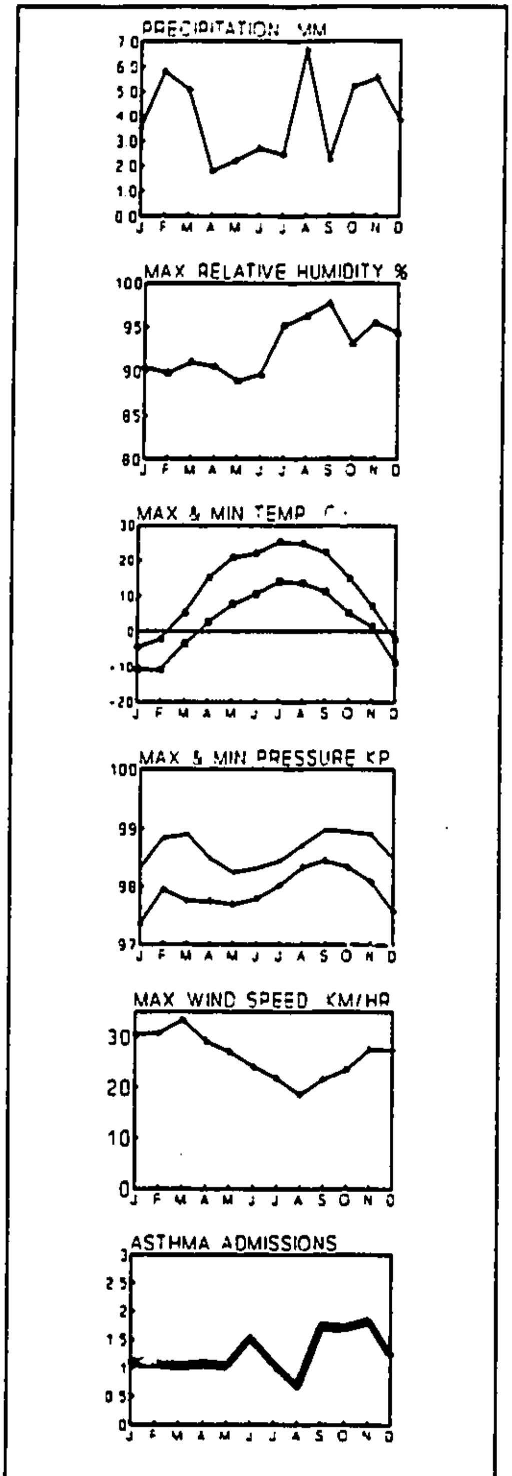


Figure 16. 1985 Monthly Means of Daily Asthma Admissions and Daily Weather Measurements

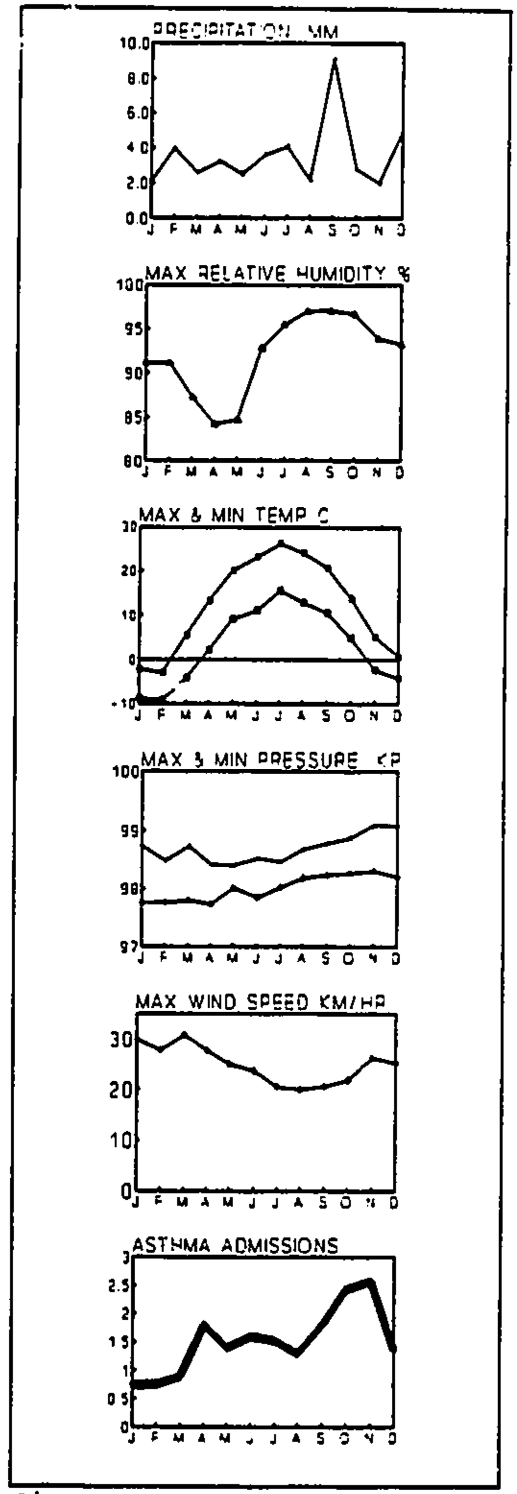


Figure 17. 1986 Monthly Means of Daily Asthma Admissions and Daily Weather Measurements

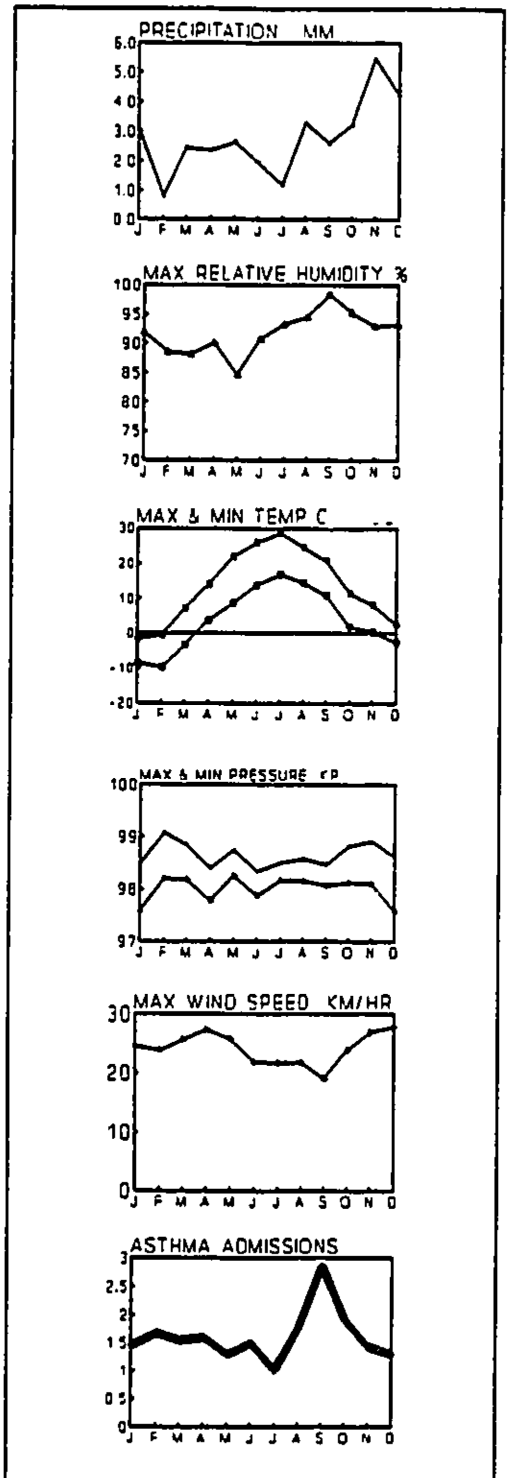


Figure 18. 1987 Monthly Means of Daily Asthma Admissions and Daily Weather Measurements

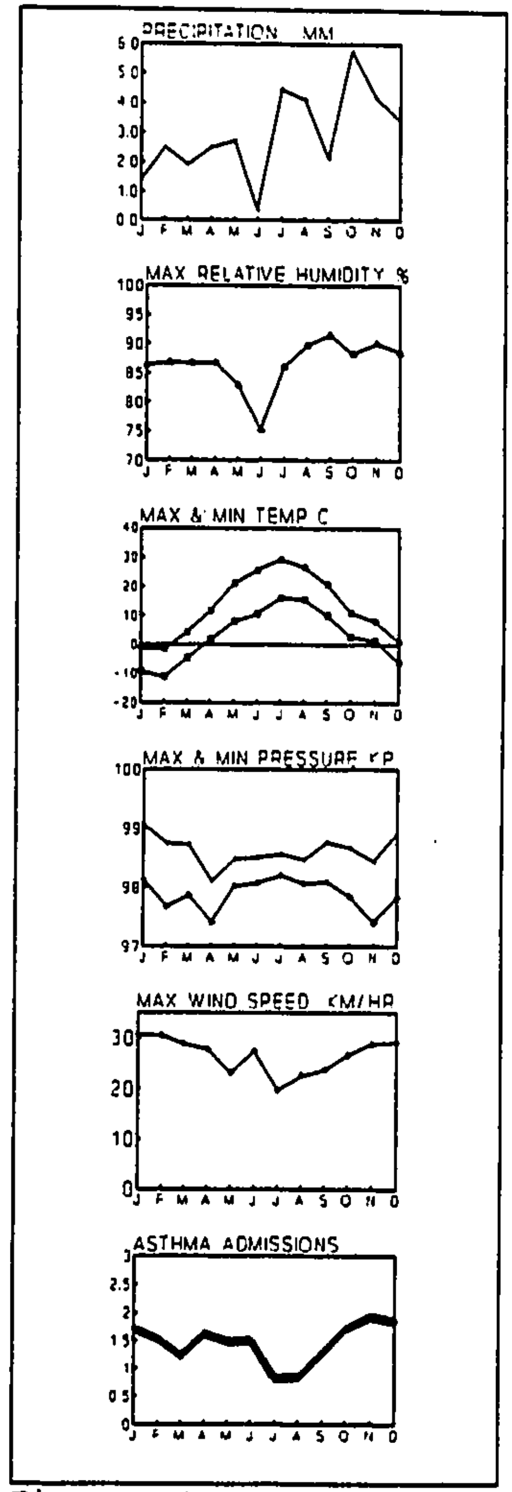


Figure 19. 1988 Monthly Means of Daily Asthma Admissions and Daily Weather Measurements

CORRELATIONS BETWEEN ENVIRONMENTAL VARIABLES:

Daily. Table IV shows correlations between same-day measurements of meteorological variables, ambient pollutants and pollens during the months of March to July over the six years. Both tree and grass pollen correlated with temperature, O_3, SO_4, and NO_3. Temperature was positively correlated with ozone and SO_4 and a negatively correlated with SO_2 which is consistent with the seasonal patterns that these variables followed. There were inter-correlations between the pollutants.

Weekly. Table V shows Spearman rank correlations between weekly averages of daily pollutant, weather, and pollen measurements. Tree and grass pollens showed a significant positive correlation with temperature, wind and with ozone. Tree pollen also correlated with NO_2 and NO_3. Weather variables were inter-correlated as were pollutants. Grass and tree pollen showed a negative correlation during the overlap of their seasons.

Table IV Correlation Coefficients Between Daily Measurements of Environmental Variables March-July

	Max-Pres	Mean Temp	Max Hum	Precip	SO_4	NO_3	Max SO_2	Max NO_2	Max O_3	Trees	Grass
Max-Pres		-.1612 **	-.2854 **	-.2319 **	ns	ns	.1428 **	.0837 **	ns	ns	ns
Mean Temp			.1600 **	ns	.3589 **	.1127 **	-.1915 **	.0862 **	.6623 **	.1973 **	.3408 **
Max Hum				.3238 **	.0948 *	ns	ns	ns	ns	-.0940 *	ns
Precip					ns	ns	ns	ns	ns	ns	ns
SO_4						.5057 **	.1329 **	.3231 **	.5775 **	.1194 **	.1444 **
NO_3							.2229 **	.4533 **	.2833 **	.1678 **	.1027 **
Max SO_2								.1912 **	ns	ns	ns
Max NO_2									.2569 **	.2174 **	ns
Max O_3										.1212 **	.3021 **
Trees											-.1982 **
Grass											

* $p < 0.01$
** $p < 0.001$
ns not significant

Table V SPEARMAN CORRELATION COEFFICIENTS BETWEEN WEEKLY MEANS OF ENVIRONMENTAL VARIABLES.

	Max-Pres	Max Temp	Max Hum	Precip	SO_4	NO_3	Max SO_2	Max NO_2	Max O_3	Trees	Grass
Wind Speed	-.1809 **	-.3400 **	-.2034 **	.2009 **	-.1532 **	-.1532 **	ns	-.2453 **	-.2487 **	.1638 *	.0883 ns
Max-Pres		ns	-.2375 **	-.3152 ***	ns	ns	ns	ns	ns	ns	ns
Mean Temp			.2406 **	-.1658 *	.4957 ***	ns	-.3128 ***	ns	.8847 ***	.2430 **	.3951 ***
Max Hum				.4485 ***	.2207 **	ns	ns	ns	ns	ns	ns
Precip					ns	ns	ns	ns	-.1748 *	ns	ns
SO_4						.5522 ***	ns	.2178 **	.5019 ***	ns	.1968 *
NO_3							.2399 **	.5238 ***	.1787 *	.2162 *	ns
Max SO_2								.2390 **	-.1923 *	-.1899 *	ns
Max NO_2									ns	.2209 *	ns
Max O_3										.2480 **	.3786 ***
Trees											-.6318 ***
Grass											

* $p < 0.01$
** $p < 0.001$
ns not significant

CORRELATIONS OF ADMISSIONS WITH POLLEN, WEATHER, AND POLLUTANTS:

Daily. Figures 20, 21 and 22 show scatter diagrams of daily emergency asthma admissions versus daily tree pollen, grass pollen and total pollen counts respectively. Admissions values are proportions which have been calculated from the ratio of observed admissions to the mean number of admissions for the same weekday during the months March-July of the same year. Spearman rank correlation coefficients are shown in each plot. Small but highly significant positive correlations were found for asthma admissions with tree pollen and total pollen counts lagged 1 and 2 days. No significant correlations were found for admissions with grass pollen.

The above correlations are also shown in Table VI along with the correlations of other environmental variables with daily admissions (asthma and non-respiratory). A very small positive correlation between asthma and the previous days wind speed existed. No positive correlations were found between asthma admissions and any pollutant, however negative correlations with SO_4, NO_3 and SO_2 were seen. Non-respiratory admissions showed a very small correlation only with ozone lagged 2 days.

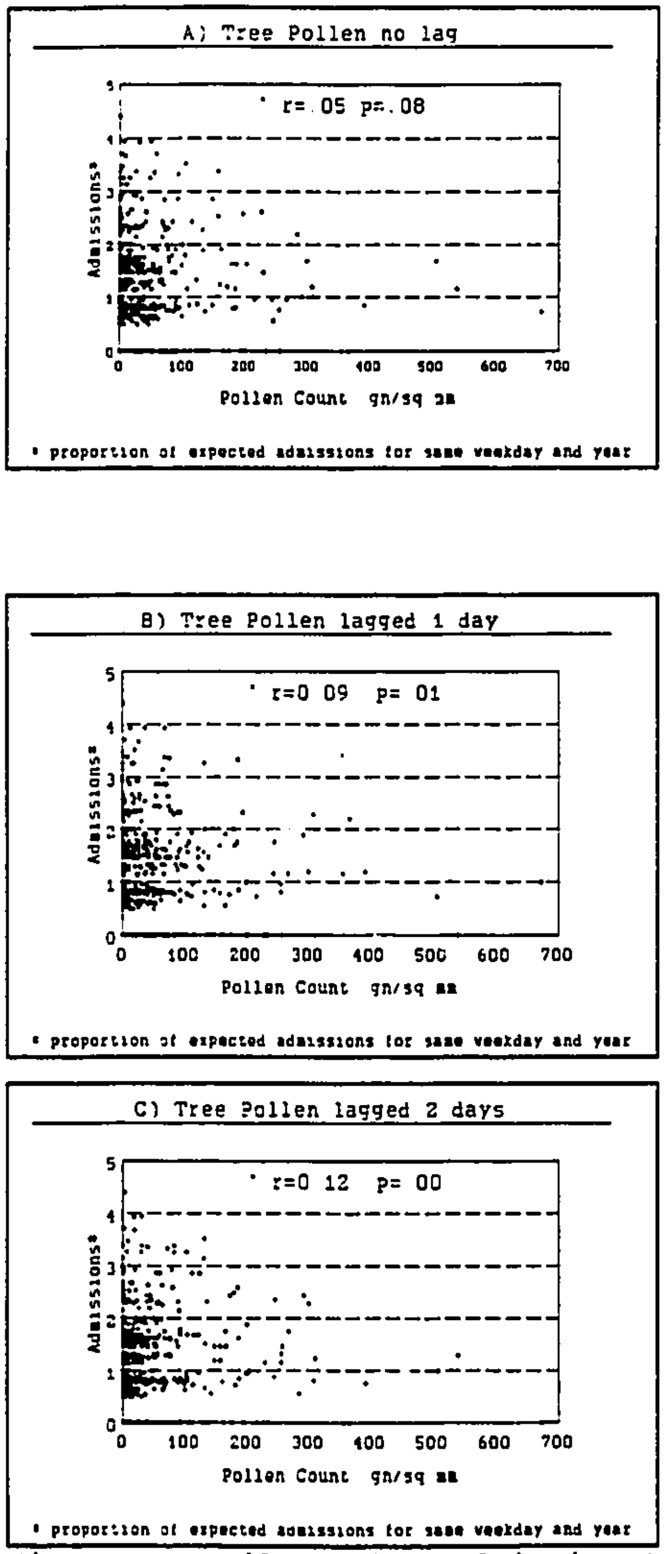


Figure 20 Daily Asthma Admissions* vs Daily Tree Pollen Count lagged 0 days (A), 1 day (B), and 2 days (C).

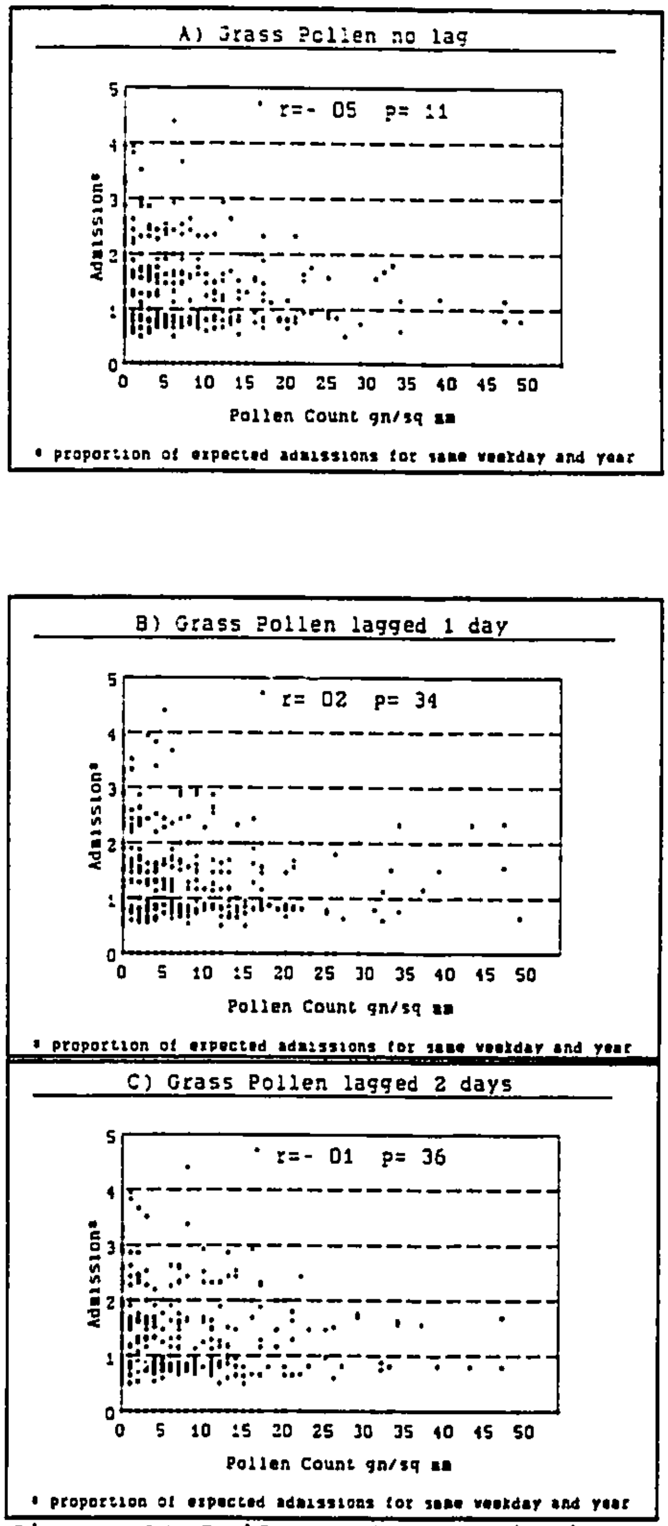
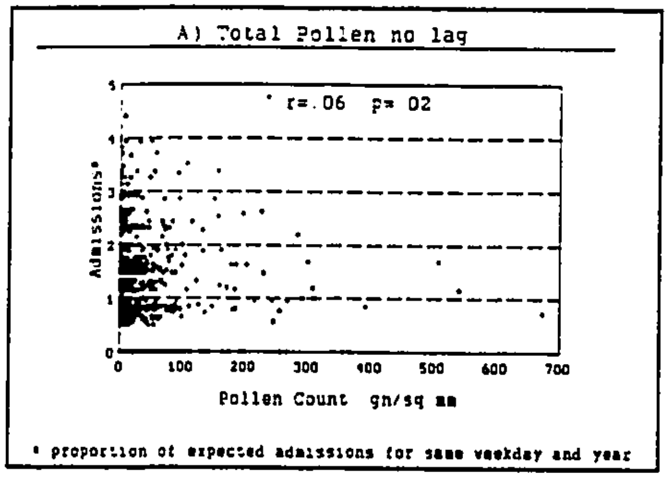
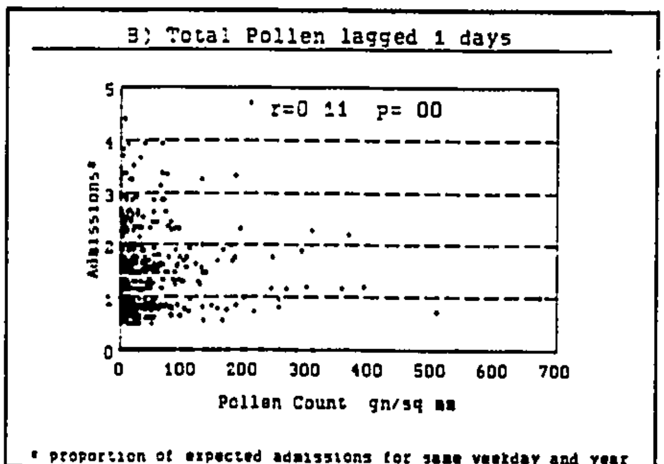


Figure 21 Daily Asthma Admissions* vs Daily Grass Pollen Count lagged 0 days (A), 1 day (B), and 2 days (C).





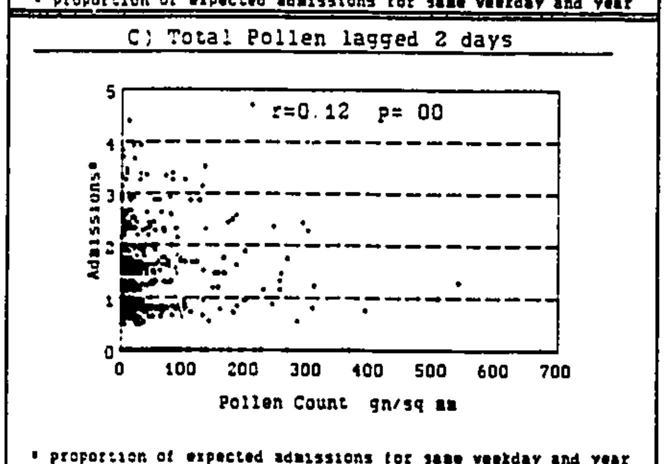


Figure 22 Daily Asthma Admissions* vs Daily Total Pollen (tree+grass) Count lagged 0 days (A), 1 day (B), and 2 days (C).

Table VI DAILY SPEARMAN RANK CORRELATIONS BETWEEN ADMISSIONS AND ENVIRONMENTAL VARIABLES.

		ASTHMA	NON-RESPIRATORY
WINDSPEED	LAG 0 days	-.0406 *(.110)*	-.0113 *(.367)*
	LAG 1	.0925 *(.003)* **	.0294 *(.188)*
	LAG 2	.0028 *(.466)*	-.0053 *(.436)*
MEAN TEMP	LAG 0	-.0306 *(.177)*	-.0026 *(.464)*
	LAG 1	.0204 *(.269)*	-.0006 *(.493)*
	LAG 2	-.0297 *(.184)*	.0267 *(.211)*
MAX HUMIDITY	LAG 0	-.0008 *(.490)*	.0288 *(.193)*
	LAG 1	-.0280 *(.198)*	-.0263 *(.214)*
	LAG 2	.0120 *(.359)*	.0108 *(.373)*
PRECIPITATION	LAG 0	.0221 *(.226)*	.0477 *(.090)*
	LAG 1	.0093 *(.396)*	-.0336 *(.172)*
	LAG 2	-.0377 *(.143)*	.0089 *(.401)*
SO4	LAG 0	-.0300 *(.182)*	-.0056 *(.433)*
	LAG 1	-.0523 *(.057)*	-.0305 *(.180)*
	LAG 2	-.1075 *(.001)* **	.0430 *(.098)*
NO3	LAG 0	.0041 *(.450)*	.0343 *(.151)*
	LAG 1	-.0237 *(.240)*	.0064 *(.423)*
	LAG 2	-.0681 *(.020)* **	.0560 *(.064)*
SO2	LAG 0	-.0742 *(.014)* **	.0289 *(.198)*
	LAG 1	-.0407 *(.115)*	.0247 *(.234)*
	LAG 2	-.0477 *(.079)*	-.0214 *(.265)*
NO2	LAG 0	.0249 *(.230)*	.0134 *(.346)*
	LAG 1	-.0023 *(.473)*	-.0269 *(.214)*
	LAG 2	-.0322 *(.170)*	.0535 *(.060)*
O3	LAG 0	.0027 *(.468)*	.0009 *(.490)*
	LAG 1	.0163 *(.313)*	-.0132 *(.347)*
	LAG 2	-.0328 *(.164)*	.0628 *(.031)* **
TREE POLLEN	LAG 0	.0530 *(.077)*	.0382 *(.153)*
	LAG 1	.0894 *(.008)* **	.0465 *(.106)*
	LAG 2	.1167 *(.001)* **	.0363 *(.166)*
GRASS POLLEN	LAG 0	-.0521 *(.111)*	.0007 *(.493)*
	LAG 1	.0178 *(.340)*	-.0287 *(.254)*
	LAG 2	-.0153 *(.361)*	.0510 *(.121)*
TOTAL POLLEN	LAG 0	.0626 *(.029)* **	.0279 *(.201)*
	LAG 1	.1051 *(.001)* **	.0246 *(.231)*
	LAG 2	.1157 *(.000)* **	.0514 *(.067)*

** - significant correlations (*p values*)

Weekly. Figures 23, 24 and 25 show scatter diagrams of weekly emergency asthma admissions versus weekly tree pollen, grass pollen and total pollen counts respectively. Spearman rank correlations were significant between weekly asthma admissions and the week's tree and total pollen count.

Table VII shows the weekly asthma-pollen Spearman rank correlations after stratification by age. Correlations are also shown for asthma with weekly weather and pollutant measurements. Asthma admissions (except in the over 35 age group) showed small to moderate correlations with tree pollen and total pollen, but not with grass. Weekly asthma admissions also showed positive correlations with wind speed and negative correlations with temperature and SO_4. Although not quite significant, ozone showed a small correlation with admissions in the 35 and older age group.

Table VIII shows these correlations for non-respiratory admissions. No significant associations were found.

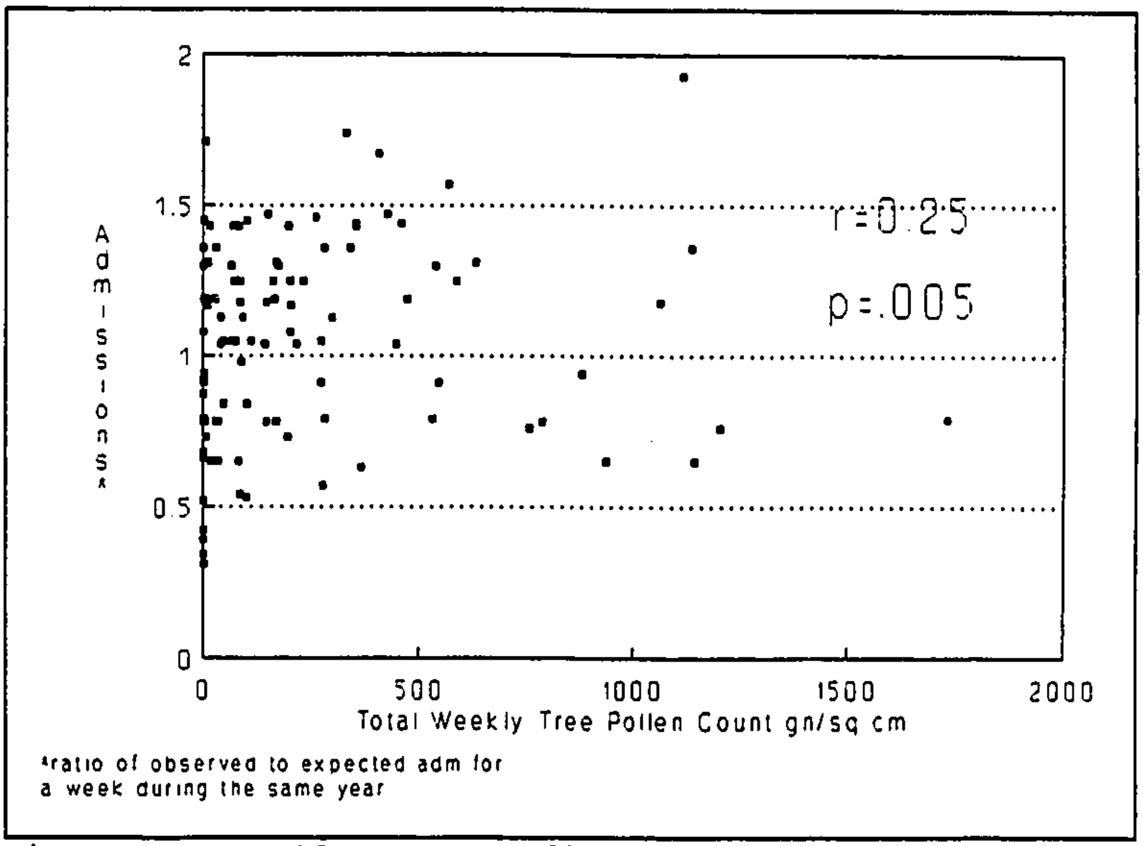


Figure 23 Weekly Tree Pollen Count vs Weekly Asthma Admissions*.

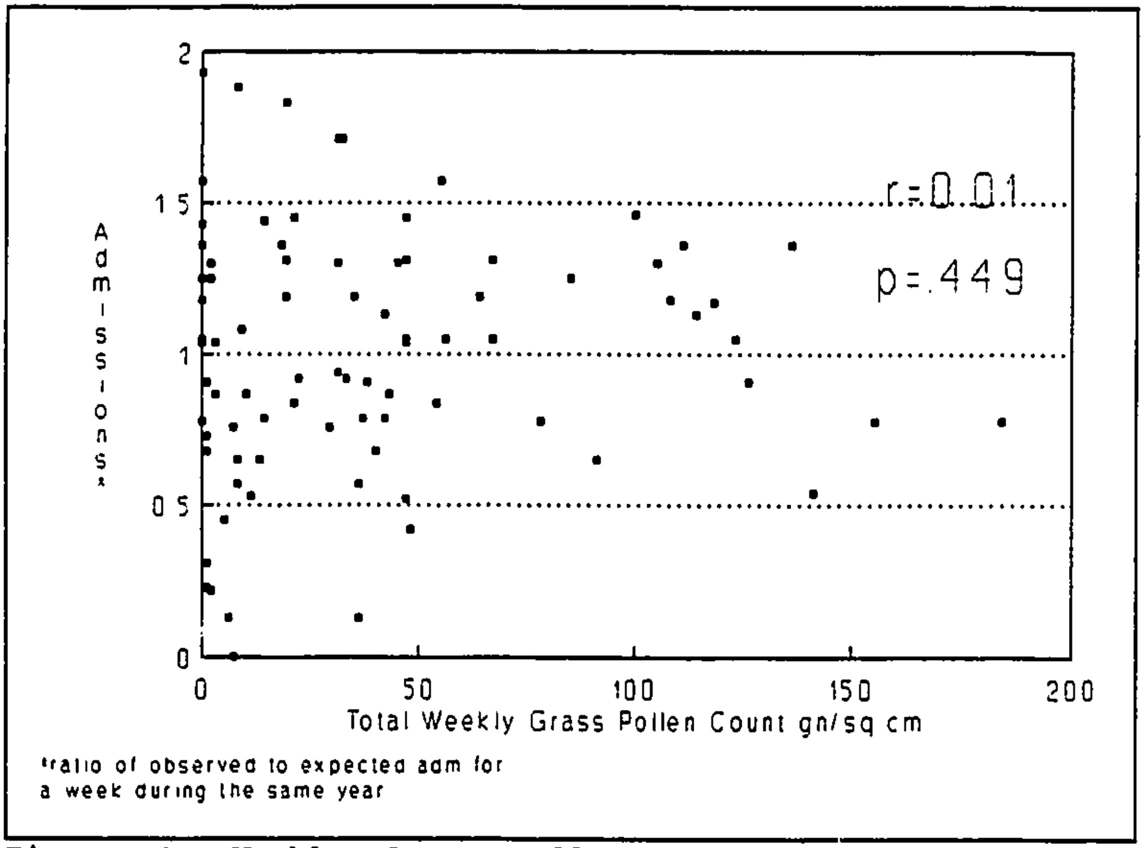


Figure 24 Weekly Grass Pollen Count vs Weekly Asthma Admissions*.

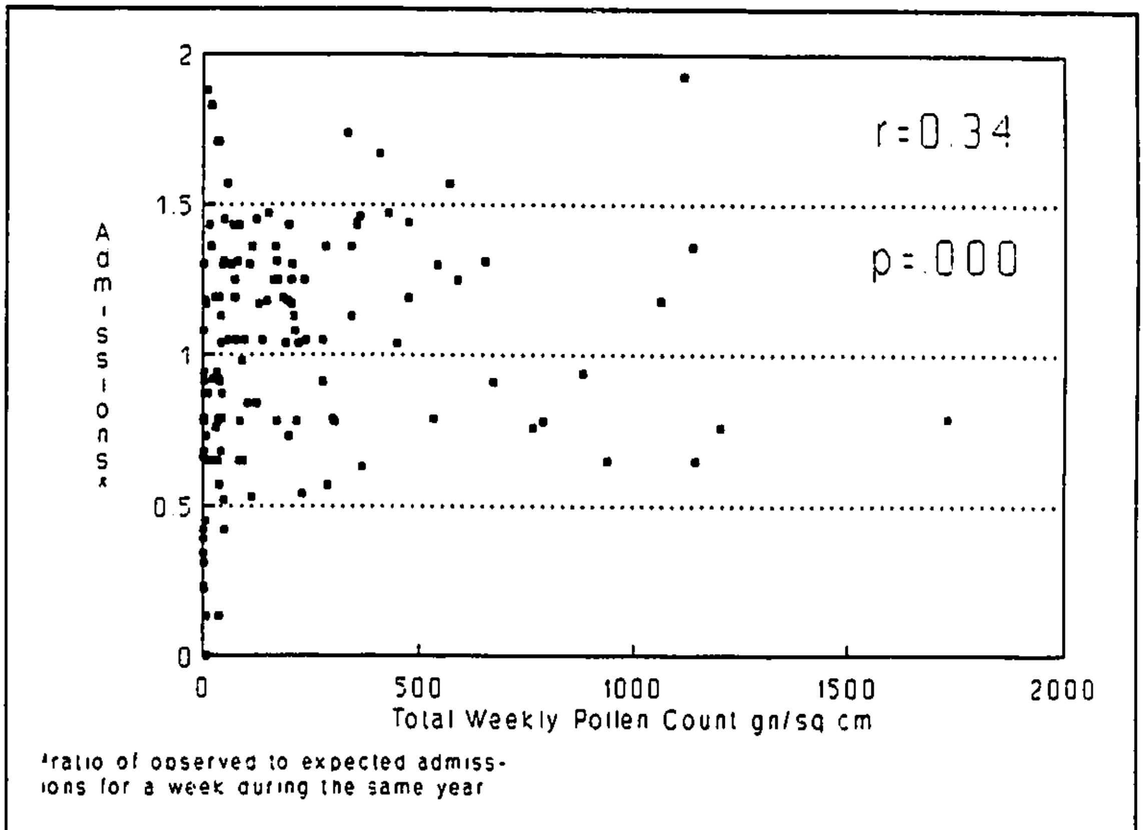


Figure 25 Weekly Total Pollen Count (tree + grass) vs Weekly Asthma Admissions*.

Table VII Spearman Rank Correlations Between Weekly Asthma Admissions and Weekly Means of Daily Environmental Variable Measurements

AGE	LT 5	5-34	35 +	ALL AGES
WINDSPEED	.1536 ** (.038)	-.0004 (.498)	.2479 ** (.002)	.1455 ** (.044)
BARO PRESSURE	-.0526 (.270)	-.0652 (.244)	.0440 (.304)	-.0627 (.233)
TEMP	-.1837 ** (.016)	.1050 (.110)	-.2241 ** (.004)	-.0848 (.161)
HUMIDITY	-.1032 (.114)	.0756 (.189)	-.1142 (.091)	-.0448 (.301)
PRECIPITATION	.1300 (.064)	.0690 (.211)	.0724 (.199)	.1576 ** (.032)
SO4	-.1334 (.059)	.0328 (.351)	-.2116 ** (.006)	-.1517 ** (.032)
NO3	.0017 (.492)	-.0159 (.427)	-.0333 (.349)	-.0781 (.181)
SO2	-.0302 (.363)	-.0749 (.191)	.0592 (.245)	-.0717 (.202)
NO2	.0563 (.257)	.0820 (.170)	.0738 (.196)	.0807 (.174)
O3	-.1050 (.110)	.1309 (.060)	-.0644 (.226)	.0332 (.349)
TREE POLLEN	.2635 ** (.003)	.1756 ** (.035)	.0644 (.254)	.2477 ** (.005)
GRASS POLLEN	-.1209 (.137)	.0250 (.411)	.1175 (.143)	.0141 (.449)
TOTAL POLLEN	.3094 ** (.000)	.2008 ** (.009)	.2031 ** (.008)	.3364 ** (.000)

** significant correlations   (*p values*)

Table VIII Spearman Rank Correlations Between Weekly Non-Respiratory Admissions and Weekly Means of Daily Environmental Variable Measurements

	NON-RESPIRATORY
	r (*p values*)
WINDSPEED	.0074 (*.467*)
BARO PRESSURE	-.0854 (*.171*)
TEMP	-.0138 (*.439*)
HUMIDITY	-.0469 (*.301*)
PRECIPITATION	-.0857 (*.170*)
SO4	.0205 (*.410*)
NO3	.0816 (*.182*)
SO2	.0001 (*.500*)
NO2	.0298 (*.371*)
O3	.0391 (*.332*)
TREE POLLEN	.0709 (*.239*)
GRASS POLLEN	.0771 (*.251*)
TOTAL POLLEN	.0693 (*.220*)

ANOVA: ASSOCIATIONS OF ADMISSIONS WITH CATEGORIZED POLLEN COUNTS:

Daily ANOVA. Daily tree, grass, and total pollen counts have been categorized into quartiles in Table IX, Table X, Table XI respectively. For each pollen category the mean daily emergency asthma admission value is shown. These values are the observed to expected admissions ratios for the same weekday and year.

Table IX DAILY ASTHMA ADMISSIONS BY TREE POLLEN QUARTILES

Daily Tree Pollen Count	# of Days	Daily Asthma Admissions ♦ -Mean Values *(S.D.)* Same Day	Pollen Lagged 1 Day	Pollen Lagged 2 Days
0 gn/cm2	212	0.9353 *(.8491)*	0.8947 *(.8080)*	0.8882 *(.8407)*
1 - 9	155	1.0444 *(.9160)*	1.0215 *(.9094)*	1.0087 *(.8939)*
9 - 37	182	1.0830 *(.8440)*	1.0588 *(.9256)*	1.0000 *(.8613)*
38 ≤	179	1.0604 *(.9340)*	1.1126 *(.8919)*	1.1903 *(.9287)*
p values				
ANOVA		0.3440	0.0864	0.0093
KRUSKALL-WALLIS		0.2482	0.0762	0.0068
LINEAR CONTRAST		0.148	0.016	0.002

♦ Admission values are expressed as ratio of observed to expected admissions for the same weekday during the months March-July of the same year.

For tree pollen (Table IX) and total pollen (Table XI), asthma admissions were lowest in the lowest quartile and became higher in higher quartiles. These trends (tested by linear contrast) were significant when the pollens were lagged 1 or 2 days. Mean non-parametric ranks of daily asthma admissions (not shown) also showed a trend from lowest in the bottom quartile to higher for the higher quartiles. ANOVA and Kruskall-Wallis test showed that admissions were significantly different between the pollen groups when the pollens were lagged 1 or 2 days.

Table X DAILY ASTHMA ADMISSIONS BY GRASS POLLEN QUARTILES

		Daily Asthma Admissions ♦ - Mean Values (S.D.)		
Daily Grass Pollen Count	# of Days	Same Day	Pollen Lagged 1 Day	Pollen Lagged 2 Days
0 gn/cm2	167	1.0535 (.8803)	0.9674 (.8525)	1.0432 (.8542)
1 - 3	128	1.0371 (.9387)	1.0388 (.8868)	1.0506 (.9165)
4 - 9	131	1.0280 (.8881)	1.0577 (.9225)	0.8747 (.8209)
10 ≤	124	0.8856 (.6735)	0.9491 (.7321)	1.0203 (.7782)
p values				
ANOVA		0.3581	0.6715	0.2801
KRUSKALL-WALLIS		0.7215	0.8319	0.2945
LINEAR CONTRAST		0.112	0.910	0.444

♦ Admission values are expressed as the ratio of observed to expected admissions for the same weekday during the months March-July of the same year.

Between grass pollen categories (Table X) there was no trend in asthma admission values. Both Analysis of Variance and Kruskall-Wallis test showed no significant difference between the quartiles.

Table XI DAILY ASTHMA ADMISSIONS BY TOTAL POLLEN COUNT (Grass + Tree) QUARTILES

		Daily Asthma Admissions ♦ - Mean Values *(S.D.)*		
Daily Total Pollen Count	# of Days	Same Day	Pollen Lagged 1 Day	Pollen Lagged 2 Days
≤1 gn/cm2	231	0.9946 *(.8527)*	0.8711 *(.8319)*	0.9372 *(.8900)*
2 - 10	239	0.9607 *(.9284)*	0.9929 *(.8838)*	0.8663 *(.8117)*
11 - 34	226	1.0350 *(.8188)*	0.9996 *(.8761)*	1.0662 *(.8874)*
35 ≤	218	1.0673 *(.8926)*	1.1237 *(.8785)*	1.1423 *(.8836)*
p values				
ANOVA		0.3825	0.0239	0.0028
KRUSKALL-WALLIS		0.1719	0.0165	0.0025
LINEAR CONTRAST		0.090	0.003	0.001

♦ Admission values are expressed as the ratio of observed to expected admissions for the same weekday during the months March-July of the same year.

Table XII shows daily non-respiratory admission mean values by total pollen quartiles. No trend in admissions was seen between pollen quartiles at any of the lags. None of the tests were significant.

Table XII DAILY NON-RESPIRATORY ADMISSIONS BY TOTAL POLLEN COUNT QUARTILES

Daily Total Pollen Count	# of Days	Daily Non-Respiratory Admissions ♦ - Mean Values *(S.D.)* Same Day	Pollen Lagged 1 Day	Pollen Lagged 2 Days
≤1 gn/cm²	231	0.9768 *(.4936)*	0.9766 *(.4830)*	0.9584 *(.4807)*
2 - 10	239	1.0349 *(.5419)*	1.0467 *(.5689)*	1.0339 *(.5558)*
11 - 34	226	1.0256 *(.5137)*	0.9789 *(.4742)*	1.0167 *(.5089)*
35 ≤	218	0.9501 *(.4798)*	0.9986 *(.5007)*	0.9799 *(.4881)*
p-values				
ANOVA		0.2548	0.4259	0.3896
KRUSKALL-WALLIS		0.3775	0.8463	0.6492
LINEAR CONTRAST		0.564	0.990	0.762

♦ Admission values are expressed as the ratio of observed to expected admissions for the same weekday during the months March-July of the same year.

Weekly ANOVA. Weekly ANOVAs of asthma admissions are shown in Table XIII, Table XIV, and Table XV for tree, grass, and total pollen respectively. The asthma admissions values are the observed to expected admission ratios for a week within the March-July period of the same year. Asthma admissions (except the 35 and over group) became higher as both tree and total pollen counts became higher. These trends - as tested by linear contrast - were all significant. Mean non-parametric ranks of asthma admissions (not shown) also increased with higher tree and total pollen quartiles. ANOVA and Kruskall-Wallis test indicated that admissions were significantly different between tree pollen groups when all age groups were combined. Admissions were also significantly different (except in the 5-34 group) between total

Table XIII WEEKLY ASTHMA ADMISSIONS BY WEEKLY TREE POLLEN COUNT QUARTILES (MARCH - JUNE)

Weekly Tree Pollen Count	# of weeks	Weekly Asthma Admissions § - Mean Values *(S.D.)*			
		< 5 yrs	5 - 35 yrs	35 + yrs	All Ages
0 - 5 gn/mm2	27	0.8401 *(.7705)*	0.8255 *(.5230)*	0.9618 *(.5128)*	0.8781 *(.3521)*
6 - 89	27	1.1473 *(.8944)*	1.0097 *(.3841)*	1.1309 *(.6573)*	1.0593 *(.2680)*
90 - 293	27	1.1079 *(.8669)*	0.9447 *(.4577)*	1.2287 *(.5866)*	1.0884 *(.2709)*
294 ≤	27	1.3559 *(.7900)*	1.2070 *(.6640)*	1.0442 *(.4946)*	1.1654 *(.3648)*
p values					
ANOVA		0.1612	0.0585	0.3509	0.0100
KRUSKALL-WALLIS		0.1022	0.0839	0.3861	0.0389
LINEAR CONTRAST		0.038	0.017	0.481	0.001

§ Admission values are expressed as the ratio of observed to expected admissions for a week during the months of March-July of the same year.

pollen groups. No significant differences or trends were seen between grass pollen quartiles.

Table XVI shows weekly non-respiratory admission mean values (observed to expected ratios for week in same year) by tree, grass, and total pollen quartiles respectively. There were no significant trends in non-respiratory admissions between tree quartiles. There was a significant positive trend in admissions between grass quartiles. A significant difference in the mean and median non-respiratory admissions existed between at least two of the total pollen quartiles, however no trend was present between the quartiles.

Table XIV WEEKLY ASTHMA ADMISSIONS BY GRASS POLLEN COUNT QUARTILES (MAY - JULY)

		Weekly Asthma Admissions § - Mean Values *(S.D.)*			
Weekly Grass Pollen Count	# of weeks	< 5 yrs	5 - 35 yrs	35 + yrs	All Ages
0 - 3 gn/mm2	21	1.1840 *(.8391)*	1.0861 *(.6221)*	0.9242 *(.6192)*	1.0433 *(.4445)*
4 - 30	21	0.8125 *(.8221)*	1.0543 *(.6596)*	0.8012 *(.6300)*	0.9262 *(.4965)*
31 - 52	21	0.9577 *(.9032)*	1.0614 *(.5709)*	0.8746 *(.4799)*	0.9864 *(.4044)*
53 ≤	21	0.9222 *(.8613)*	1.0957 *(.4942)*	1.1587 *(.6229)*	1.0820 *(.2777)*
p values					
ANOVA		0.5569	0.9951	0.2390	0.6385
KRUSKALL-WALLIS		0.4572	0.9866	0.2600	0.5831
LINEAR CONTRAST		0.446	0.951	0.182	0.663

§ Admission values are expressed as the ratio of observed to expected admissions for a Week during the months of March-July of the same year.

Table XV WEEKLY ASTHMA ADMISSIONS BY TOTAL POLLEN COUNT QUARTILES

Weekly Tree Pollen Count	# of weeks	Weekly Asthma Admissions § - Mean Values *(S.D.)* < 5 yrs	5 - 35 yrs	35 + yrs	All Ages
0 - 18 gn/mm2	35	0.6619 *(.6713)*	0.8162 *(.5842)*	0.6949 *(.5490)*	0.7462 *(.4003)*
19 - 81	34	1.0121 *(1.006)*	1.0235 *(.5085)*	1.0855 *(.6450)*	1.0387 *(.3899)*
82 - 242	35	0.9470 *(.7357)*	1.0532 *(.4458)*	1.1783 *(.5950)*	1.0910 *(.2607)*
243 ≤	34	1.3905 *(.7703)*	1.1109 *(.6420)*	1.0451 *(.5058)*	1.1289 *(.3598)*
p values					
ANOVA		0.0034	0.1334	0.0037	0.0000
KRUSKALL-WALLIS		0.0026	0.0663	0.0055	0.0002
LINEAR CONTRAST		0.001	0.031	0.010	0.0000

§ Admission values are expressed as the ratio of observed to expected admissions for a Week during the months of March-July of the same year.

Table XVI WEEKLY NON-RESPIRATORY ADMISSIONS BY TOTAL POLLEN COUNT QUARTILES

Pollen Quartile ♦	Weekly Non-Respiratory Admissions § (All Ages) -Mean (S.D.) Tree	Grass	Total Pollen
I	.9387 (.2678)	.8794 (.3528)	0.8558 (.3822)
II	1.0092 (.2037)	1.0332 (.3829)	1.0905 (.1875)
III	1.1031 (.2753)	1.0931 (.1685)	1.0572 (.2501)
IV	.9583 (.2113)	1.1010 (.3052)	0.9990 (.2367)
p value			
ANOVA	0.0640	0.0646	0.0027
KRUSKALL-WALLIS	0.1742	0.0993	0.050
LINEAR CONTRAST	0.46	0.015	0.06

§ Admissions are expressed as the ratio of observed to expected non-respiratory admissions for week during the months of March-July of the same year.

♦ Quartile Cutpoints - Tree: 5, 89, 293 Grass: 3, 30, 52 Total Pollen: 18, 81, 242.

ANALYSIS OF COVARIANCE:

Ozone, wind speed, and temperature showed associations with pollen counts (Table V) and asthma admissions (Table VIII). ANCOVA was therefore used to rule out confounding by these variables and the results are found in Table XVII, Table XVIII, and Table XIX. These tables show the ANOVA comparing pollen counts and admissions after adjusting for the confounder. An explanation of the various tests found in these tables is found at the bottom of the tables.

Zero slopes tests indicated that all three variables warranted control in the 35 and over age group, and temperature also warranted control in the under 5 age group. However, adjusting for each of these variables did not change the association between asthma admissions and pollen.

Table XVII ANCOVA: MEAN NUMBER OF WEEKLY ASTHMA ADMISSIONS BY TOTAL POLLEN COUNT QUARTILES AFTER ADJUSTMENT FOR OZONE.

		WEEKLY ASTHMA ADMISSIONS ♠ - ADJUSTED FOR OZONE ¶ MEAN VALUES			
Weekly Total Pollen Count	# of Weeks	< 5 yrs	5 - 35 yrs	35 + yrs	All Ages
0 - 18 gn/mm2	35	0.6248	0.8267	0.6558	0.7314
18 - 81	34	1.0228	1.0211	1.0957	1.0422
81 - 242	35	0.9699	1.0469	1.2021	1.0995
242 ≤	34	1.3973	1.1084	1.0525	1.1313
ANOVA FOR ADJUSTED MEANS	p	0.002	0.182	0.001	0.000
Ozone-Admissions REG.COEF •		-.0091	0.0025	-.0094	-.0034
ZERO SLOPES •	p	0.080	0.481	0.012	0.143
EQUALITY OF SLOPES ••	p	0.744	0.632	0.616	0.883
LINEAR CONTRAST	p	0.0003	0.042	0.003	0.000

♠ Admission values are expressed as the ratio of observed to expected asthma admission for a week during the months March-July of the same year.

¶ Weekly Mean of Daily Maximum Ozone.

The ANOVA and LINEAR CONTRAST tests presented are after adjustment for Ozone.

• The Ozone-Admissions regression coefficient is shown. The test of significance for this regression is the ZERO SLOPES. A significant zero slopes test indicates that controlling for ozone in the analysis is warranted.

•• The EQUALITY OF SLOPES test checks if the ozone-admission regression slope is the same between all 4 pollen groups. A test that is not significant indicates that the slopes are the same and the ANCOVA is therefore valid.

Table XVIII ANCOVA: MEAN NUMBER OF WEEKLY ASTHMA ADMISSIONS BY TOTAL POLLEN COUNT QUARTILES AFTER ADJUSTMENT FOR WIND SPEED.

		Weekly Asthma Admissions ♦ - Adjusted for Wind Speed ¶ MEAN VALUES			
Weekly Total Pollen Count	# of Weeks	< 5 yrs	5 - 35 yrs	35 + yrs	All Ages
0 - 18 gn/mm2	35	0.6703	0.8120	0.7089	0.7497
18 - 81	34	1.0276	1.0158	1.1131	1.0466
81 - 242	35	0.9398	1.0573	1.1647	1.0869
242 ≤	34	1.3767	1.1180	1.0187	1.1210
ANOVA FOR ADJUSTED MEANS	p	0.005	0.119	0.005	0.000
REGRES. COEF *		0.0117	-.0064	0.0221	0.0065
ZERO SLOPES *	P	0.358	0.462	0.015	0.252
EQUALITY OF SLOPES **	p	0.239	0.447	0.203	0.601
LINEAR CONTRAST	p	0.001	0.025	0.025	0.000

♦ Admission values are expressed as the ratio of observed to expected asthma admissions for a week during the months March-July of the same year.

¶ Weekly Mean of Daily Maximum Wind Speeds.

The ANOVA and LINEAR CONTRAST tests presented are after adjustment for wind speed.

* The wind speed - Admissions regression coefficient is shown. The test of significance for this regression is the ZERO SLOPES. A significant zero slopes test indicates that controlling for wind speed in the analysis is warranted.

** The EQUALITY OF SLOPES test checks if the wind speed - admission regression slope is the same between all 4 pollen groups. A test that is not significant indicates that the slopes are the same and the ANCOVA is therefore valid.

Table XIX ANCOVA: MEAN NUMBER OF WEEKLY ASTHMA ADMISSIONS BY TOTAL POLLEN COUNT QUARTILES AFTER ADJUSTMENT FOR TEMPERATURE.

		WEEKLY ASTHMA ADMISSIONS ♦ - ADJUSTED FOR TEMPERATURE ¶ MEAN VALUES			
Weekly Total Pollen Count	# of Weeks	≤ 5 yrs	5 - 35 yrs	35 + yrs	All Ages
0 - 18 gn/mm2	35	0.6038	0.8394	0.6229	0.7232
18 - 81	34	1.0554	1.0071	1.1372	1.0546
81 - 242	35	0.9787	1.0408	1.2171	1.1029
242 ≤	34	1.3772	1.1156	1.0296	1.1237
ANOVA FOR ADJUSTED MEANS	p	0.001	0.211	0.000	0.000
Temp-Admissions REG. COEFF •		-.0018	0.0007	-.0022	-.0007
ZERO SLOPES •	P	0.042	0.244	0.000	0.084
EQUALITY OF SLOPES ••	p	0.478	0.675	0.397	0.365
LINEAR CONTRAST	p	0.000	0.042	0.003	0.000

♦ Admission values are expressed as the ratio of observed to expected asthma admissions for a week during the months March-July of the same year.

¶ Weekly Mean of Daily Minimum Temperatures.

The ANOVA and LINEAR CONTRAST tests presented are after adjustment for Temperature.

• The Temperature-Admissions regression coefficient is shown. The test of significance for this regression is the ZERO SLOPES. A significant zero slopes test indicates that controlling for temperature in the analysis is warranted.

•• The EQUALITY OF SLOPES test checks if the temperature-admission regression slope is the same between all 4 pollen groups. A test that is not significant indicates that the slopes are the same and the ANCOVA is therefore valid.

MULTIPLE REGRESSION ANALYSIS:

A multiple regression analysis was carried out treating weekly admissions as the dependent variable and entering weekly measurements of all the environmental variables as covariates. Pollen was treated categorically (categories 1-4). This analysis showed essentially the same results as the ANCOVA results (ie the relationship between pollen and admissions persists despite controlling for confounders). However because of the categorical nature of the pollen, it was felt that the ANCOVA results were more suitable and the regression results are therefore not presented here.

STRATIFICATION BY POLLEN COUNT:

Table XX shows Spearman rank correlations of weekly asthma admissions with weekly pollutants and weather variables after stratification by total pollen count. When the pollen count was greater than its median, asthma admissions were negatively correlated with SO_4 and NO_3. There were no significant positive correlations of asthma admissions with any of the pollutants regardless of whether the week's pollen count was greater or less than the median. A negative correlation of temperature with asthma admissions became larger and significant when pollen counts were above the median.

Table XX Spearman Rank Correlations Between Weekly Asthma Admissions and Pollutants, Stratified by Pollen Count

	POLLEN COUNT ≤81 §	POLLEN COUNT >81 §
SO4	-.0083 (.473)	-.3293 (.003) **
NO3	.0869 (.240)	-.3677 (.001) **
SO2	-.0254 (.480)	-.0106 (.466)
NO2	.1806 (.070)	-.1862 (.065)
O3	.0324 (.396)	-.0979 (.212)
Min. Temp	-.0273 (.412)	-.3044 (.005) **
Min Humidity	.0240 (.422)	-.0769 (.265)
Max Wind	.0607 (.310)	.1705 (.081)
** significant correlations	(p values)	

§ Pollen count during same week

D. DISCUSSION:

SEASONAL TENDENCY:

The data in this study suggest that, on average over 6 years, asthma hospitalizations rose during the months March-June and again during the months September-November. The latter increase was larger. These results were not tested statistically for seasonality however and it therefore can not be concluded that increases during the above months are significant. However such a finding would be consistent with the findings of Mao et al[6] and others[7,8,9,10] who have shown asthma morbidity peaks in the spring and fall.

Tree and grass pollen were consistently present during the spring months. Their peak months also varied from year to year. However tree pollen generally peaked in April or May and grass pollen peaked in June each year.

DAILY AND WEEKLY ASSOCIATIONS BETWEEN ADMISSIONS AND POLLEN:

This study showed that daily and weekly emergency asthma admissions during the spring were associated with tree pollen counts. Asthma admissions were also associated with total pollen (grass and tree combined) but not with grass pollen alone. Considerably higher total tree pollen than grass pollen counts may partly explain why asthma admissions were associated with tree but not with grass. There was also an overlap between tree and grass pollen seasons such that tree pollen was elevated during May and early June when grass was still low. Grass related asthma admissions should therefore have been low in May. However asthma admissions would actually have been high because of tree pollen. This would give the appearance that asthma admissions were elevated whether grass pollen was high or low. Any association between grass and asthma admissions may have been masked in this way.

Size of associations. Although significant, both daily and weekly correlations of asthma admissions with tree pollen and total pollen were small (Spearman coefficients up to 0.12 daily and 0.33 weekly). This suggests that the effect that pollen has on asthma admissions, although significant is small. However three other explanations may account for the small sizes.

Firstly, the study was ecological in design. It is not possible to determine pollen levels that individuals were exposed to. An attempt was made to include only individuals who could have been exposed to the pollen levels measured by omitting from the study those who were either not residents of London or not admitted to a hospital within the London area. However, even if an individual had the potential to be exposed, his or her actual exposure would be dependent upon such factors as the amount of time spent outdoors[14].

Secondly, the lack of correlation size might also be attributed to the semi-quantitative nature of gravitationally collected pollen counts[46]. Pollen counts were therefore divided into quartiles and categorical analyses were done. From lowest to highest total pollen quartiles there was a 33 percent increase in mean admissions on a daily basis and a 32 percent increase on a weekly basis.

Thirdly, pollen of individual species could not be considered separately because only aggregated tree and grass pollen counts were available. Some species may have low allergenicity and their inclusion into the aggregate could have had a diluting effect. On the same token, highly allergenic species might have shown a larger association with asthma admissions if they could have been assessed separately.

Lag Effect. For daily analyses, the association between asthma admissions and pollen counts tended to be largest and most significant when pollen was lagged by one or two days prior to admissions. Asthmatics exposed to pollen allergen in experiments can respond with both an immediate deterioration in respiratory function and, in some individuals, a delayed response hours later[13]. The findings from this study would support the theory that an ongoing delayed response is important in bringing about an admission to hospital. It is also possible that the lag is a result of a delay between the time of pollen exposure and initial symptoms and the time an individual actually goes to hospital and is admitted.

Differences by Age Groups. The association between weekly asthma admissions and pollen counts varied by age group. Tree pollen levels were significantly associated with admissions in the less than 5 age group and the 5 to 34 years age group, but showed no association with the age 35 and over group. There are two possible explanations for the weaker association between pollen and asthma admissions in the older age group.

Firstly, other conditions such as chronic bronchitis, emphysema, and congestive heart failure are sometimes misdiagnosed as asthma in adulthood because they may demonstrate airway obstruction and wheezing[49]. However they are not allergic disorders. Misdiagnosis may therefore weaken any association between allergenic pollen and asthma admissions in this older age group.

Secondly, atopy may actually be less prevalent in older asthmatics than in younger ones. This was shown by Hendrick et al[50] who skin prick tested 656 asthmatic patients with the allergens of pollens, moulds, house dust, *D. farinae* (dust mite), animal danders, and foods. Of those patients who had first developed symptoms of asthma under the age of ten, 94 percent had positive skin reactions to at least one allergen. In those that were over 30 years when asthma first presented, only 67 percent had positive skin reactions. This supports the suggestions of others that extrinsic, atopic asthma is often early in onset whereas intrinsic, nonatopic asthma is more often late in onset[49].

Control of Confounders. In this study the potential for confounding by ozone, temperature and wind on the association between asthma and pollen was identified. **Ozone** rises during the spring similar to pollen, and has been shown to affect asthma admissions in other studies. **Wind** is important to pollination[12] but may also cause circulation of other factors that exacerbate asthma such as pollutants, smoke, and dust. **Temperature** has been related to asthma symptoms[37] and is also important to plant pollination[12]. All three of these potential confounders were associated with both pollen and asthma admissions during the study. Other potential confounders that were being considered in the study did not show the associations with both pollen and admissions.

After controlling for each of these three potential confounders, the association between asthma admissions and pollen remained. Therefore the association between asthma admissions and pollen could not be explained by confounding environmental variables.

Non-Respiratory Admissions. Non-respiratory admissions were associated with grass and total pollen on a weekly basis only. The association of these admissions with pollen is probably spurious for three reasons. Firstly, there was no trend (ie no dose response) in non-respiratory admissions between total pollen quartiles as there was for asthma admissions. Secondly, the associations were found only on a weekly and not on a daily basis. And thirdly, there is no biologically plausible mechanism to explain a cause-effect relationship between non-respiratory admissions and pollen exposure.

Effect Modification. The relationship between temperature and asthma admissions was modified by pollen. After stratification by pollen count, a negative correlation between asthma and temperature was only present when the pollen count was high.

Possibly, therefore, it is the combination of cooler temperatures and higher pollen counts that is important in elevating asthma admissions. This could explain why an association was found with tree pollen - present earlier in the spring when temperatures are cooler - and not with grass pollen.

Nonspecific bronchial responsiveness, which has been reported by others after pollen exposure[13], might be important in the relationship between pollen, temperature, and asthma admissions. After pollen exposure, the airways of asthmatics become more responsive to the affects of other factors such as temperature. Thus temperature might have more of an effect on asthma morbidity when pollen counts are high.

This study failed to show a significant positive modification of the effect of pollutants on asthma admissions by previous pollen exposures. The presence of effect modification for pollutants would also have supported the role of heightened non-specific bronchial responsiveness. The lack of an effect here may be because pollutant levels were generally not high enough to have a noticeable effect on admissions during the study months (see below).

ASSOCIATIONS OF ADMISSIONS WITH POLLUTANTS AND WEATHER:

Pollutants. No significant *positive* associations of asthma admissions with any pollutant were found on either a daily or weekly basis in this study. Ozone came close to significance at the 95% level when correlated with weekly admissions in the over 35 age group. Significant *negative* correlations of asthma admissions were found for SO_4 on a weekly basis and for SO_4 and NO_3 on a daily basis. These negative correlations are not biologically plausible. These findings could be explained on the basis of confounding by temperature. Both SO_4 and NO_3 are positively correlated with temperature and temperature is negatively correlated with asthma admissions. However because temperature and pollutants were not the exposures of primary interest in this study, adjustment for this possible confounded relationship was not undertaken. A more extensive study looking at pollutants - possibly using time series analysis - may help clarify this.

It must be noted though that these negative correlations are not in concordance with the findings of other ecological studies. In fact most have found positive correlations between pollutants (O_3, SO_4, and SO_2) and asthma admissions. In Bates study of Southern Ontario[32], hospital asthma admissions were found to have small but significant correlations with O_3, SO_4, and SO_2 during the summer, but not during the winter. In Levy's one year study in Hamilton, Ontario[33] strong correlations were found for weekly total respiratory admissions (asthma, bronchitis, bronchiolitis, emphysema and pneumonia) at 4 hospitals with the weekly air pollution index (an index of SO_2 and COH) and with SO_2 levels. The correlations grew stronger the closer the hospital was to a steel factory which was the major source of pollution. Therefore, O_3, SO_2, and SO_4 have previously shown positive correlations with asthma specifically or respiratory admissions more generally in Southern Ontario.

This lack of positive associations of asthma with pollutants in London may be explained in part by a lack of statistical power because of a small number of admissions. In London, weekly admission during this study period fell in the range of 4-17. This compares with 16-56 weekly respiratory admissions during Levy's study in Hamilton[33] and a mean of 15.8 asthma admissions per day in Bates study of Southern Ontario[32].

It is also possible that **pollutant levels were not high enough** to affect asthmatics during the study period. This is suggested by the following:

Ozone: In this study the maximum hourly ozone value recorded during the spring over the six years was 128 ppb. Exposure of asthmatics to levels of 200 ppb in experimental conditions have resulted in no change in respiratory function[40]. It appears that only repeated exposure to higher levels (350 ppb) or single exposures to extremely high levels (ie 600 ppb) will result in significant changes in pulmonary function[30].

Bates[32] found significant associations of ozone with asthma admissions only during the summer months, and not during the winter. Ozone reaches its highest levels during July and August, so it is possible that this is the only time of year (not winter, spring, or fall) that this pollutant is high enough in Southern Ontario to affect asthmatics.

Sulphur Dioxide: Airway resistance in asthmatics exposed to SO_2 levels as high as 500 ppb in experimental conditions has not increased unless these individuals were exercised as well[38]. In sensitive asthmatics though, levels of 100 ppb in combination with exercise has increased airway resistance. Nevertheless these SO_2 levels were higher than the 80 ppb maximum value recorded during this study.

Levy's study in Hamilton[33] found a significant association between respiratory admissions and SO_2. Although Levy did not report the levels of SO_2 that were measured, it is likely - given the sources of SO_2 in Hamilton - that they would have been considerably higher than in London. In fact annual means of SO_2 reported by the Ontario Ministry of Environment were 2 to 3 times higher in Hamilton than London during the years 1980 to 1989[31].

Sulphate: Sulphate levels in London reached a maximum of 44.69 $\mu g/m^3$ during the study period over the six years. Levels of SO_4, like ozone, tend to peak during the summer months. It was only during the summer months that Bates found a correlation of this pollutant with asthma admissions[32]. Thus again it is possible that levels were not high enough to have an appreciable positive effect on asthma admissions in London during this study.

Nitrogen Dioxide: The maximum value of NO_2 recorded during the study period over the six years was 120 ppb. Levels of 100 ppb have been shown to slightly increase airway resistance and nonspecific airway reactivity[43]. Hence, it would be possible that the exposures on high NO_2 days could have affected sensitive asthmatics during this study period. Nitrogen dioxide levels, however, vary considerably by proximity to source of pollutant (such as traffic routes)[31]. This lack of geographic stability most probably would account for the absence of association of NO_2 with asthma admissions.

Weather. Asthma admissions showed a negative correlation with **temperature** on a weekly basis, but not on a daily basis. A negative association is consistent with some ecological studies[51,28,36,33] but not others[32,34]. In experiments, the inspiration of cold air has been shown to reduce FEV1[52] and increase airway resistance[37]. The association found in this study is therefore plausible.

However, this study also found that the association between temperature and asthma admissions was present only when pollen counts were high (as discussed above). It may therefore be that natural exposure to cool temperature is not enough on its own to seriously exacerbate asthma (ie to the point that hospitalization is sought). Other factors such as pollen that affect the airways may also have to be present.

Wind speed showed small positive correlations with asthma admissions on a weekly and daily basis (when lagged one day). This finding is consistent with other ecological studies[36,28, 51]. Because windspeed is associated with pollen release, this correlation could be due to confounding by pollen. In this study, pollen counts showed only a weak correlation with windspeed. A complicating factor is the unpredictable adverse effect that wind has on gravitational sampling methods[47] that were used to measure pollen for this study.

LIMITATIONS AND METHODOLOGICAL DIFFICULTIES:

Ecological design. This study was ecological in design and the associations that were found may be useful in generating further hypotheses. However it is not possible to conclude that these associations were causal because it can not be ascertained that individuals were exposed to the measured pollen levels.

The ecological nature of this study also prevented considering other factors that are known to be important to asthma such as cigarette smoking, exercise etc. It is possible that some of these may interact with pollen. It is also possible that some of these could act as confounders. For example, during the spring when weather improves more people may exercise. It may be this increase in exercise that exacerbates asthma and not pollen which is coincidently present.

A panel study in the future could help to answer some of these concerns. In such a study asthmatics could carry personal pollen samplers. Personal diaries would also allow consideration of other factors that cannot be addressed in an ecological study (eg is it necessary to exercise or hyperventilate in order for pollen to have an effect?).

Unavailable Data. Data was not available in this study for particulate matter or for moulds. Both particulate matter and moulds have been shown in previous ecological work to be related to asthma hospital admissions[25]. Their importance to spring time asthma emergency admissions in London remains unknown.

Individual pollen species data was not available. Therefore potentially important species could not be identified in this study.

Hospital Admissions as an Indicator of Morbidity. Emergency hospital admissions were used in this study for three reasons. Firstly, it has been shown by Mao et al that asthma hospitalizations - not other levels of asthma morbidity - increase during the spring months in Ontario. Secondly, reliable data on hospital admissions is readily available from the Hospital Morbidity Records Institute (H.M.R.I.). And thirdly, emergency admissions to hospital would be an indicator of *acute* problem which could be a result of acute changes in the environment. For these reasons, asthma emergency hospital admissions were the best choice for an outcome variable in this study.

Emergency admissions to hospital however are only a limited indicator of actual asthma morbidity that is occurring at any given time in the population. Some individuals may be seen and treated in emergency rooms without being admitted[34], and others may be able to manage acute exacerbations of asthma at home.

Nevertheless, emergency hospital admissions would indicate the level of severe morbidity that is present.

Repeat Admissions. An individual could have accounted for more than one admission in the H.M.R.I. data set over the study period. Therefore the total number of 1163 admissions during the spring of the 6 study years does not indicate the actual number of individuals who required admission. However use of admissions rather than individuals gives an indication of the level of morbidity in the asthmatic population on an ongoing basis.

Misclassification. Misclassification between asthma and other respiratory diseases because of misdiagnoses is a possibility particularly for younger and older age groups[49]. Such misclassification would be random in that there is no reason to suspect that a physician would be more likely to make an incorrect diagnosis on days when pollen counts are high than on days when the counts are low. Such random misclassification would have had a diluting effect on associations. Therefore it is possible that small associations between asthma admissions and pollutants could have been missed. The associations between pollens and asthma admissions, however would only have been stronger than found if such misclassification played an important role.

Adjustment for Annual and Weekday Trends. It was necessary to account for annual trends and variations in asthma admissions by weekday. This was done by determining the ratio of observed admissions on a given day to the mean number of admissions for the same weekday during March-July of the same year. The mean admission value (the denominator of ratio) would necessarily include days that had high admissions as a result of high pollen. The estimated associations between proportional deviations and pollens would therefore be a conservative one.

E. CONCLUSIONS:

Emergency asthma admissions in London, Ontario during the months of March through June in the years 1983-88 were significantly associated with tree and total pollen counts on both a daily and weekly basis. This finding along with the previous knowledge that pollen can clinically exacerbate asthma[13], suggests that pollen may contribute to the spring peak in asthma morbidity. Further studies which have consistent results will help to determine if the association between pollen and asthma admissions is causal.

The most significant associations were found in the under 35 age groups, in which atopy may be more prevalent.

Temperature was negatively associated with weekly asthma admissions. The association was larger when pollen counts were elevated. This suggests that pollen may modify the effect that cool temperature has on asthma admissions.

Significant positive associations were not found between asthma admissions and any of the pollutants examined in this study. A possible reason is that pollutant levels were not high enough in London during the study months to have a significant effect.

Even though causality could not be addressed in this study, the consistent association between tree pollen and asthma suggests that those asthmatics who are sensitive to tree pollen should be managed with particular care during the spring.

Further ecological studies may be warranted to confirm the findings of this investigation and to address some of the methodological problems that were encountered. In particular, a study in a larger population (ie Metropolitan Toronto) for a longer period of time (ie a decade) would help improve statistical power.

Further studies could also include volumetrically collected pollen counts. These counts would be more quantitative, and would allow consideration of the pollen from individual species. Such a sampling method could also provide data on fungal spores for analysis.

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