

Associations Between Atmospheric Concentrations of Spores and Emergency Department Visits for Asthma Among Children Living in Montreal

Marie Raphoz, MSc; Mark S. Goldberg, PhD; Michelle Garneau, PhD;
Léa Héguy, MSc; Marie-France Valois, MSc; Frédéric Guay, MSc

ABSTRACT. The authors carried out a time-series study to determine whether short-term increases in the concentrations of spores were associated with emergency department visits from asthma among children 0 to 9 years of age in Montreal, 1994–2004. Concentrations of spores were obtained from one sampling monitor. The authors used parametric Poisson models to model the association between daily admissions to emergency rooms for asthma and ambient exposures to a variety of spores, adjusting for secular trends, changes in weather, and chemical pollutants. For first admissions and exposures to *Basidiomycetes*, the authors found positive associations at all lags but the concurrent day. For *Deuteromycetes* and *Cladosporium*, risks were positive starting at lag 3 days and diminished at lag 6 days. There was little evidence of associations for readmissions, except for *Basidiomycetes*. The results indicate that *Basidiomycetes* and *Cladosporium* spores may be implicated in the exacerbation of asthma among children, most notably in the case of first-time visits to emergency departments, and that the effects appear to be delayed by several days.

KEYWORDS: epidemiology, outdoor air pollutants, pediatric asthma, spores, time-series study

Asthma and various other allergic diseases are considered to be the most prevalent health conditions worldwide.¹ In 2005, the global prevalence of asthma was about 300 million and there were about 255,000 deaths attributed to asthma. It has been predicted that in the next decade deaths from asthma will increase by 20%.^{2,3} In Canada, the prevalence of asthma (1996–1997) was approximately 7.4%, and 10% of those afflicted were children.⁴

The etiology of asthma is multifactorial with a genetic predisposition and an environmental component.^{1,5,6} Environmental triggers include seasonal aeroallergens (eg, pollen), colds and influenza, indoor mildew, animal hair and dander, and household dust.^{1,7,8}

Airborne spores are the reproductive cells of mushrooms and there are about 100,000 different species.^{9,10} Airborne spores can trigger respiratory diseases because the structure

Marie Raphoz and Michelle Garneau are with the Department of Geography at Université du Québec à Montréal in Montreal, Quebec, Canada; Mark S. Goldberg, Léa Héguy and Marie-France Valois are with the Marie-France Valois Department of Medicine at McGill University in Montreal, Quebec, Canada; and with the Division of Clinical Epidemiology at McGill University Health Centre in Montreal, Canada. Frédéric Guay is with the Consortium Ouranos sur la climatologie régionale et l'adaptation aux changements climatiques in Montréal, Québec, Canada.

of the proteins makes them allergenic and their small size permits them to become lodged in the airways and alveoli of the lungs.^{11,12} As a result of such exposures, asthma may develop or be exacerbated in sensitive individuals.¹³

Concentrations of airborne spores are influenced by weather conditions and can attain levels 100 to 1,000 times higher than those of pollen.¹⁴ Increasing temperatures may extend the sporulation period, thereby providing longer time intervals for exacerbating allergic symptoms. Concentrations of spores in North America generally peak between the spring and autumn and they are correlated with increasing temperature, so that in a “warm” year production of spores can begin earlier and extend longer than usual.^{15–20} Moreover, because cities are generally hotter than the surrounding countryside, sporulation can begin earlier in urban areas as compared to rural areas.

There have been only a handful of studies used to investigate associations between spores and asthma.^{11,21–26} We conducted the present study to determine whether concentrations of *Basidiomycetes*, *Ganoderma*, *Deuteromycetes*, and *Cladosporium* spores were associated with visits to emergency departments for asthma among children 0 to 9 years of age living in Montreal, Quebec, Canada, between 1994 and 2004. We have previously published results from this study regarding associations with grass and weed pollen.⁷

METHODS

Description of the data

The study included children, 0 to 9 years of age, living on the Island of Montreal who were admitted for asthma (code 493 of the 9th revision of the International Classification of Diseases) to emergency departments of hospitals in the city.³ (Montreal has slightly less than 2 million inhabitants living in an area of about 500 km² [2001]).²⁷ Emergency department visits were identified from records of the universal Quebec health insurance plan. There are only 2 pediatric hospitals and 1 adult acute care hospital in Montreal that serves pediatric asthmatics and almost all of the visits were to these institutions. Asthma was defined according to the initial assessment of the attending emergency physician. These data have 100% coverage, as all children in Quebec are registered with the Quebec health insurance plan.

Each admission record was identified by a unique, denormalized identifying number, so we were able to distinguish initial and subsequent visits to emergency departments. In the analysis, we distinguished between first visits and readmissions.

Concentrations of spores were determined using a GRIPST-2000 rotary impact sampler of the Aerobiology Research Laboratory, an Ontario-based private company that manages the Canadian national network of aeroallergen collectors. The sampler is located approximately 1 km north of the Saint Lawrence River on the western part of the island, and it was installed 2.45 m above the ground.

The spore collection period is generally from April 1st to October 31st of each year. Some observations were below the limit of detection in the beginning of spring and at the end of autumn, probably due to early or late freezing periods, which are known to suppress the production of spores.²¹ During the collection period, spores were collected every morning at 08:00 and species were identified. Concentrations were thus based on an average of the previous 24 hours, beginning at 08:00. The 4 types of spores *Basidiomycetes* spp., *Ganoderma* spp., *Deuteromycetes* spp., and *Cladosporium* spp. predominate in terms of quantity and allergenicity and these were selected for analyses.^{21–23}

The weather data were provided by the Meteorological Service of Canada from their monitoring station located at the Pierre Elliott Trudeau International Airport (Latitude: 45°28'05"N; Longitude: 73°44'29"W) situated approximately 30 km west of downtown Montreal. In the analyses, we made use of maximum and minimum daily temperature, maximum air pressure, and change in maximum air pressure over the previous 24 hours. Twelve air pollution monitors distributed over the Island provided hourly concentrations of ozone (O₃) and nitrogen dioxide (NO₂). Ozone was measured using ultraviolet absorption and NO₂ was measured using chemical luminescence. There was considerable missing data for particles (PM_{2.5}) and thus we did not consider this pollutant in the analyses.

Statistical methods

The goal of the analyses was to estimate the association between daily numbers of emergency department visits for asthma and daily concentrations of spores. We thus used a time-series design to meet this objective.^{21,28–33} As emergency department visits for asthma are rare, we assumed that the natural logarithm of the daily number of visits was distributed as a Poisson variable. Because the data were overdispersed (greater variation in the distribution than expected by the Poisson model), we used quasi-likelihood estimation in the Generalized Linear Models (in S-PLUS; MathSoft, 2002) to model the natural logarithm of daily counts of visits as functions of the predictor variables (secular trends, concentrations of spores, air pollution, weather).^{31,34} Emergency department visits varied considerably, with important seasonal and subseasonal trends, and we thus accounted for this nuisance variable (referred hereafter as the “temporal filter”) by modeling day during the observation period using parametric natural cubic spline functions.

Our analyses were based on the period when spores were present (April 1 to October 31) across the 11 years of observation. Because subjects were identified by unique and encrypted identifiers, we analyzed these outcomes separately. Moreover, we selected a different temporal filter for initial and subsequent visits because the temporal patterns were different. For each analysis, we selected the temporal filter by varying the number of degrees of freedom (*df*) of the natural cubic spline function for day of study, so that the optimum

filter was chosen that maximized (highest *p* value) the Bartlett test for white noise.^{28,30,34} We evaluated these functions from 50 to 180 *df*. This selection also led to the least amount of serial autocorrelation, as evaluated from the partial autocorrelation function. In addition to this temporal filter, we also accounted for other temporal trends in the emergency visit data by including factors for year, month, and day of the week (referred to as the “base model”).

To account for potential confounding from daily weather conditions and concentrations of air pollution, we evaluated a series of models that added to the base model variables for daily maximum temperature, maximum barometric pressure, maximum concentration of ozone, and maximum concentration of NO₂.²⁸ These potential confounding variables were evaluated from midnight to midnight, which differed from the measurement of the spores (08:00–08:00), and were included in the statistical model at the same lag that the spores were evaluated at. The covariates were included in the models as simple linear functions or as natural cubic spline functions (from 2 to 5 degrees of freedom). We found that the linear functions produced the best fit for all potentially confounding variables (using a minimum Akaike Information Criterion [AIC]).³⁵ We also inspected visually the exposure-response functions from the natural spline functions to confirm these findings.³⁵

The findings of linearity were consistent with previous observations for air pollution but were not consistent with what is usually observed for maximum temperature, which for many health outcomes often appears as a complex function having an approximate threshold at lower temperatures and a strong increasing exponential component at higher temperatures. The linear effect in maximum temperature is, however, quite plausible because of the restricted range of observations during the year (April to October). We also evaluated whether the response functions for concentrations of the 4 types of spores were non-linear (using natural splines) and again found that a linear function best described these data.

Starting with the base model, we determined, using a minimum AIC criterion, whether daily maximum temperature, daily maximum air pressure, daily minimum temperature, and change in maximum air pressure from the previous 24 hours improved the fit. As all 4 variables reduced the AIC and because of strong correlations between the temperature and pressure variables, we developed 2 sets of adjusted models: model 1 incorporated maximum temperature and

maximum barometric pressure and model 2 included the difference in barometric pressure from the previous day and minimum temperature. We then added to each of these models the two air pollutants (NO₂, O₃).

In estimating the short-term effect of concentrations of spores on visits to the emergency department, we investigated the same day of exposure (referred to as lag 0 days) as well as lags 1 to 6 days. The potential confounding variables were evaluated on the same day as the exposure for spores. Because the concentration of spores referred to the time period ending at 08:00 on the concurrent day, lag 0 day refers to the period of exposure that included 16 hours from the previous day and 8 hours from the concurrent one.

The estimate of the association between concentrations of each type of spore and emergency department visits from asthma is presented as a mean percent change (MPC) for a change of 100 spore grains per cubic meter and associated 95% confidence interval (CI). In computing the confidence intervals, we assumed that the regression coefficient was normally distributed, with the standard error corrected for non-Poisson dispersion.^{29–31,36}

RESULTS

Over the 11-year study period, 43,780 emergency department visits were recorded, with 22,756 of these being single visits (mean of 9.67 per day) and 21,024 representing readmissions (mean of 8.93 per day) (Table 1). A decrease in the number of annual visits was observed over the study period, falling from a total of 5,156 in 1994 to 2,427 in 2004 (Figure 1).

The average distribution in concentrations of spores during the sporulation season (April to October, 1994 to 2004) is shown in Figure 2. Figure 3 shows that there was a secular increase in the number of *Basidiomycetes* and *Ganoderma* during the study period but *Cladosporium* and *Deuteromycetes* were fairly constant. Table 2 shows the distributions for spores, weather variables, and atmospheric pollutants. Amongst the 4 types of spores considered here, *Deuteromycetes* had the highest mean daily concentrations (1,533 grains/m³) and *Ganoderma* the lowest (395 grains/m³). Although Montreal has a rather temperate climate, during the study period (April to October) the daily average maximum temperature was fairly high (20.1°C).

Table 1.—Distribution of Daily Visits to the Emergency Department for Asthma Among Children Aged 0 to 9 Years in Montreal, April to October, 1994–2004

	Total number over the study period	Mean number per day	Variance	Centiles			
				25	50	75	Maximum
First visits	22756	9.67	38.57	5	8	13	39
Readmissions	21024	8.93	34.93	5	8	12	41
Total visits	43780	18.60	115.27	11	17	25	71

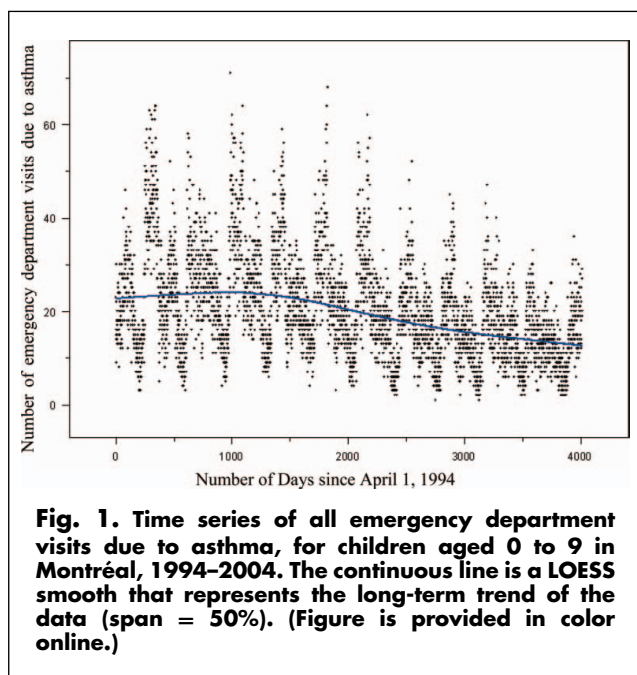
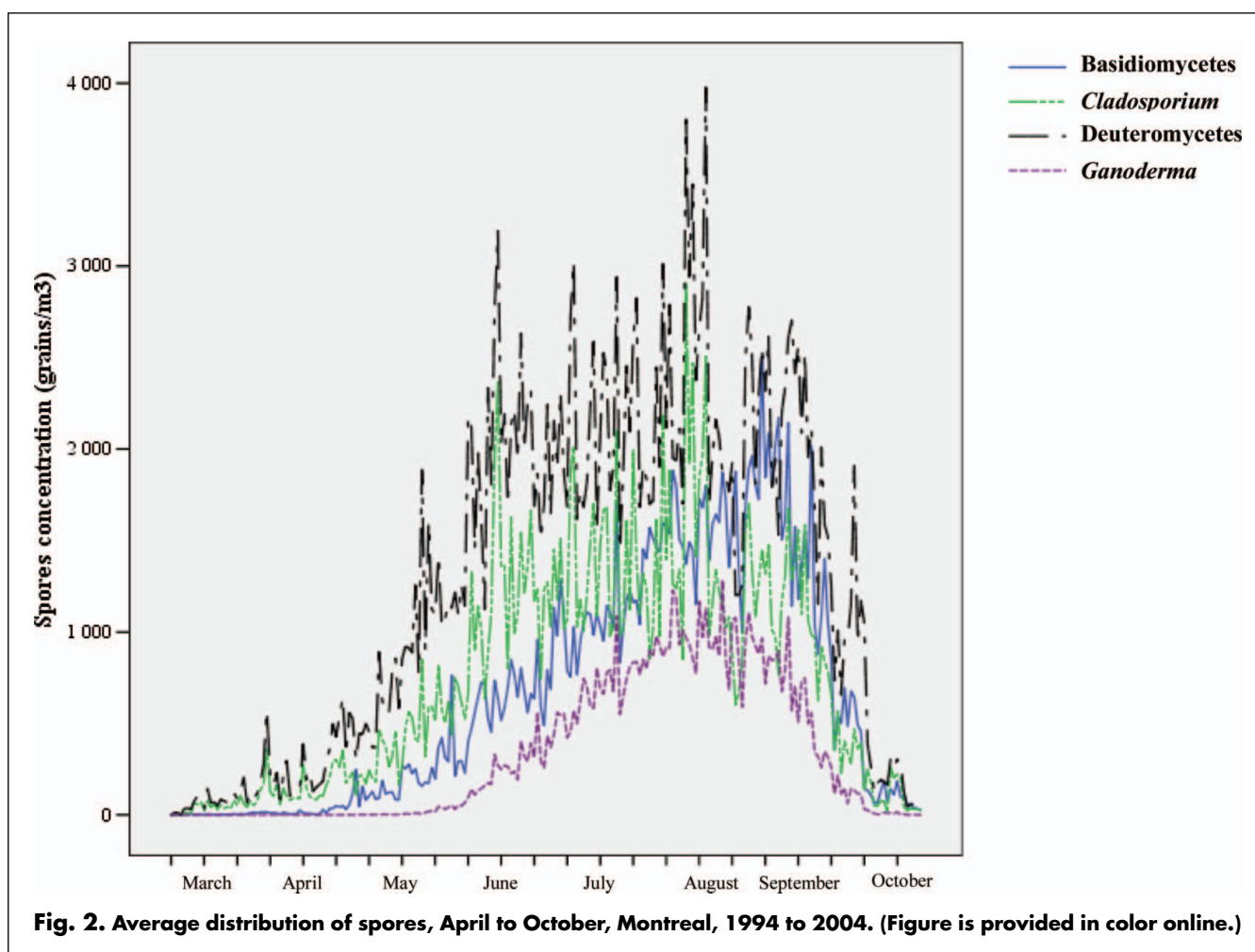


Table 3 shows the estimated associations between all visits for asthma (first and subsequent visits combined) to the emergency department and concentrations for species of spores across lags 0 to 6 days. The results are expressed as the percentage increase in admissions per increase of 100 spore grains/m³. We show results adjusted only for temporal trends as well as for 2 models adjusted for different sets of weather variables and for the 2 air pollution variables. (Recall that model 1 was adjusted for maximum temperature, maximum barometric pressure, maximum O₃, maximum NO₂; model 2 was adjusted for minimum temperature, difference in barometric pressure from the previous day, maximum O₃, maximum NO₂.) There were little differences between models 1 and 2, but in some analyses there was some evidence of confounding (differences between the base and adjusted models).

For *Basidiomycetes* spores, we found positive associations but with wide confidence intervals, except for lags 2 and 3 days in which the associations were mostly negative. Only at lag 4 days did we find a positive association for which the 95% confidence interval did not include the null (ie, model 1:



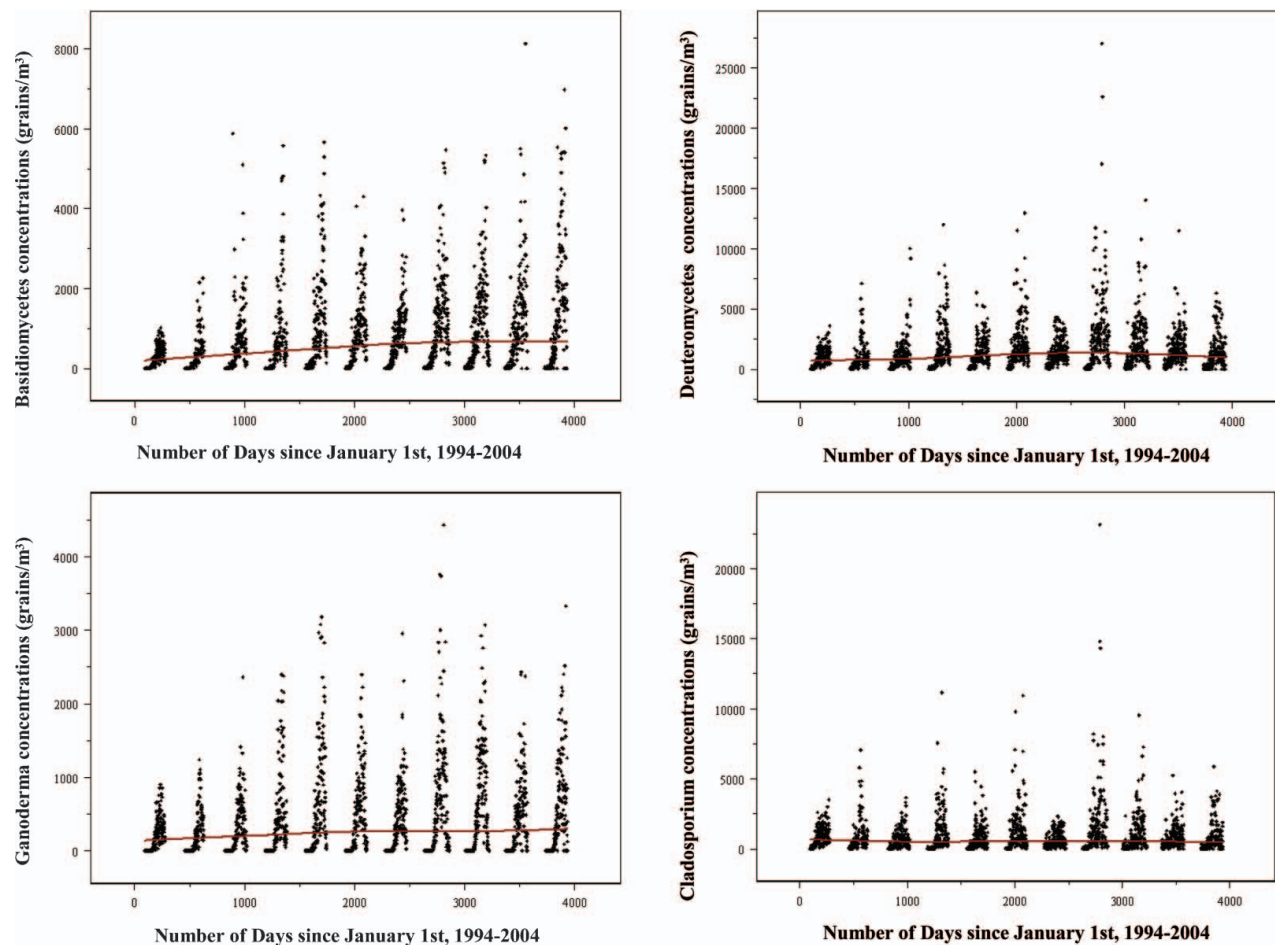


Fig. 3. Time series of all spores, from January 1, 1994, until December 31, 2004. (Figure is provided in color online.)

Table 2.—Distributions of Concentrations of Spores, Selected Weather Variables, and Pollutants, Montreal, April to October, 1994–2004

	Units	Number of days of observations	Mean	Minimum	Centiles			Maximum
					25	50	75	
<i>Basidiomycetes</i>	grains/m ³	2077	800.41	0	36.1	453.4	1153.64	8128.8
<i>Ganoderma</i>	grains/m ³	2075	395.22	0	0	153.26	595.13	4429.68
<i>Deuteromycetes</i>	grains/m ³	2076	1533.03	0	299.79	1025.10	2061.75	27017.02
<i>Cladosporium</i>	grains/m ³	2075	897.72	0	131.3	467.16	1178.06	23129.02
Maximum temperature	°C	2335	20.12	−5.10	15.20	21.40	25.70	36.20
Minimum temperature	°C	2345	9.82	−14.50	4.90	10.70	15.10	24.60
Maximum barometric pressure	mbar	2354	1013.30	992.40	1009.30	1013.10	1017.40	1036.70
Barometric pressure from previous day	mbar	2354	0.02	−18.90	−3.30	0.25	3	21.10
Maximum ozone concentration	μg/m ³	2354	91.35	16	69	88	108	299
Maximum nitrogen dioxide concentration	μg/m ³	2354	86.95	22	67	84	102	248

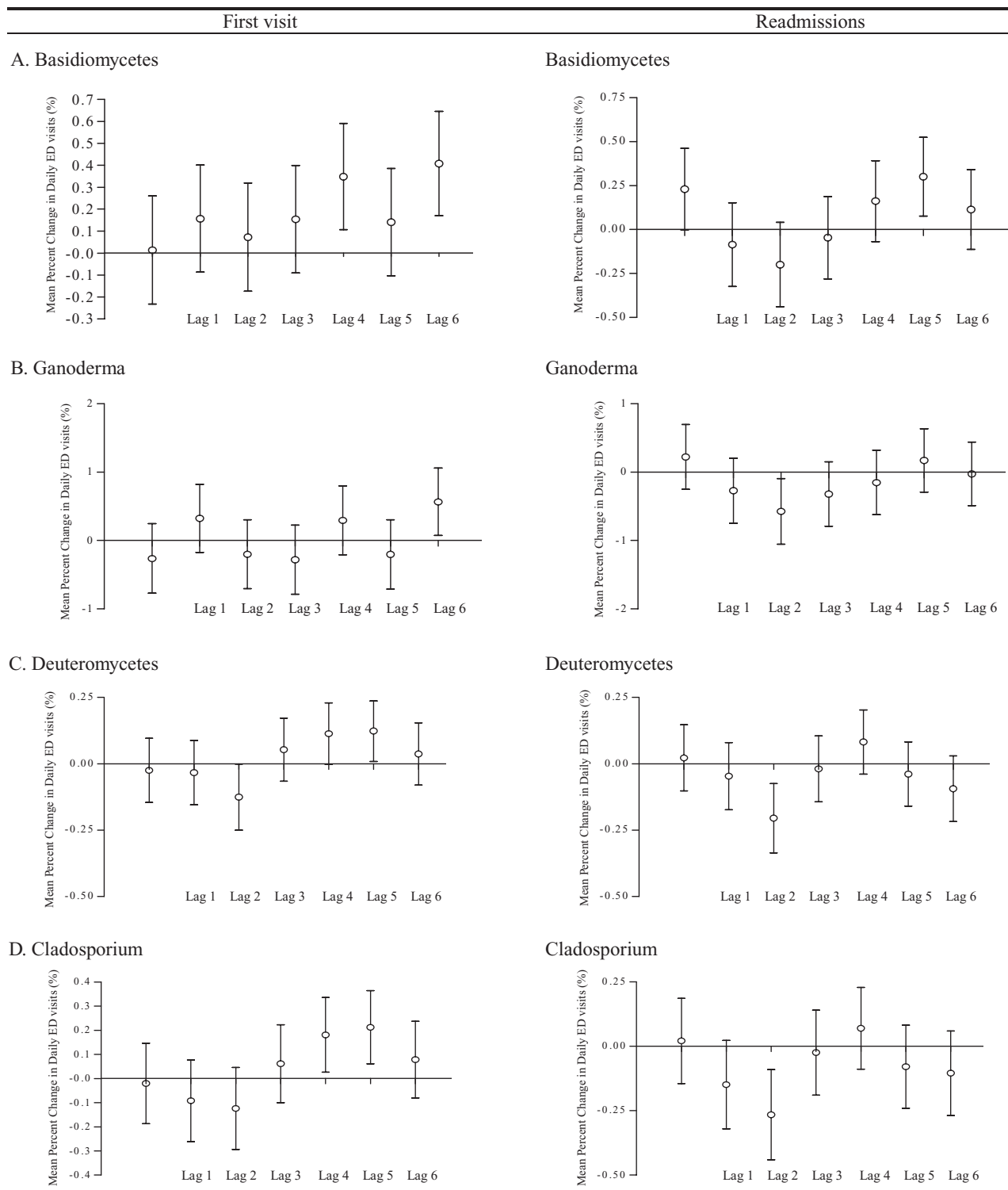


Fig. 4. Mean percent change in first visits and readmissions to emergency departments for asthma among Montreal children between April and October, 1994–2004 (adjusted as per model 1). The estimated MPC in daily emergency department visits due to asthma for an increase of 100 grains of spores/m³ is shown by the circles and the vertical bars represent the 95% confidence intervals (95% CIs).

Table 3.—Mean Percent Change in All Visits to the Emergency Department for Asthma Among Children Aged 0–9 Years, Evaluated for an Increase of 100 Spore Grains/m³, Montreal, April to October, 1994–2004

	Lag	Adjusted for temporal trends only			Model 1			Model 2		
		MPC (%)	95% CI (%)		MPC (%)	95% CI (%)		MPC (%)	95% CI (%)	
<i>Basidiomycetes</i>	0	0.14	−0.02	0.32	0.12	−0.05	0.30	0.08	−0.09	0.26
	1	0.07	−0.1	0.24	0.02	−0.15	0.21	−0.003	−0.18	0.17
	2	−0.04	−0.22	0.13	−0.08	−0.26	0.09	−0.11	−0.29	0.07
	3	0.03	−0.14	0.21	0.01	−0.16	0.19	0.009	−0.17	0.19
	4	0.2	0.03	0.37	0.19	0.01	0.36	0.22	0.04	0.40
	5	0.1	−0.06	0.27	0.14	−0.02	0.32	0.16	−0.01	0.34
<i>Ganoderma</i>	6	0.1	−0.06	0.27	0.17	−0.001	0.34	0.18	0.004	0.35
	0	0.06	−0.28	0.42	−0.01	−0.38	0.34	−0.05	−0.42	0.30
	1	0.11	−0.23	0.47	0.02	−0.33	0.38	−0.005	−0.36	0.35
	2	−0.3	−0.66	0.05	−0.40	−0.77	−0.04	−0.42	−0.79	−0.05
	3	−0.27	−0.62	0.08	−0.32	−0.68	0.03	−0.33	−0.69	0.03
	4	0.06	−0.28	0.41	0.03	−0.32	0.40	0.08	−0.28	0.44
<i>Deuteromycetes</i>	5	−0.16	−0.51	0.19	−0.05	−0.41	0.30	−0.06	−0.42	0.30
	6	0.06	−0.27	0.41	0.25	−0.10	0.60	0.22	−0.13	0.57
	0	0.02	−0.06	0.11	0.01	−0.08	0.10	−0.01	−0.11	0.07
	1	−0.01	−0.10	0.07	−0.04	−0.13	0.05	−0.06	−0.16	0.02
	2	−0.13	−0.23	−0.04	−0.17	−0.27	−0.07	−0.19	−0.29	−0.09
	3	0.02	−0.06	0.11	0.01	−0.07	0.10	0.01	−0.08	0.10
<i>Cladosporium</i>	4	0.08	−0.004	0.16	0.08	−0.009	0.17	0.09	0.003	0.18
	5	0.01	−0.07	0.09	0.03	−0.05	0.12	0.04	−0.04	0.13
	6	−0.07	−0.16	0.01	−0.03	−0.12	0.05	−0.03	−0.12	0.05
	0	0.03	−0.08	0.15	0.009	−0.11	0.13	−0.01	−0.13	0.11
	1	−0.08	−0.20	0.04	−0.12	−0.25	0.007	−0.14	−0.27	−0.01
	2	−0.15	−0.28	−0.02	−0.20	−0.33	−0.06	−0.20	−0.34	−0.07
	3	0.03	−0.08	0.15	0.02	−0.10	0.14	0.02	−0.10	0.14
	4	0.13	0.01	0.25	0.13	0.01	0.25	0.14	0.023	0.26
	5	0.04	−0.07	0.16	0.07	−0.04	0.19	0.08	−0.03	0.20
	6	−0.06	−0.18	0.05	−0.01	−0.13	0.10	−0.02	−0.14	0.10

Note. Model 1: Also adjusted for maximum temperature, maximum barometric pressure, maximum O₃, maximum NO₂. Model 2: Also adjusted for minimum temperature, difference in barometric pressure from the previous day, maximum O₃, maximum NO₂.

MPC_{lag4} = 0.19%, 95% CI: 0.01–0.36%; model 2: MPC_{lag4} = 0.22%, 95% CI: 0.04–0.40%).

The pattern of associations for *Ganoderma* was mostly negative (eg, model 2, negative associations at lags 0 to 3 days and lag 5 days), with a significant negative association observed at lag 2 days (model 1: MPC_{lag2} = −0.40%, 95% CI: −0.77%, −0.04%; model 2: MPC_{lag2} = −0.42%, 95% CI: −0.79%, −0.05%).

The pattern for *Deuteromycetes* was similar to *Ganoderma* (negative associations in model 2 at lags 0 to 2 days and at lag 6 days), with a significant negative association at lag 2 days (model 1: MPC_{lag2} = −0.17%, 95% CI: −0.27%, −0.07%; model 2: MPC_{lag2} = −0.19%, 95% CI: −0.29%, −0.09%).

The pattern for *Cladosporium* was similar again to the 2 previous types of spores, with a significant negative association found at lag 2 days (model 1: MPC_{lag2} = −0.20%, 95% CI: −0.33%, −0.06%; model 2: MPC_{lag2} = −0.20%, 95% CI: −0.34%, −0.07%) and at lag 1 day (model 2: MPC_{lag1} = −0.14%, 95% CI: −0.27%, −0.01%).

We also conducted a series of analyses separating first visits from readmissions (Figure 4). Because there were little differences between the results from model 1 and model 2,

we present only the findings from model 1. The pattern of associations for all types of spores but *Ganoderma* differed considerably from that found in Table 1, especially for first admissions. Specifically, for first admissions and exposures to *Basidiomycetes*, we found positive associations at all lags but the concurrent day. For *Deuteromycetes* and *Cladosporium*, risks were positive starting at lag 3 days and diminished at lag 6 days. Some of the associations reached statistical significance.

COMMENT

It has been recognized for nearly a century that spores play a role in exacerbating asthma.^{37,38} In most Canadian cities, exacerbations in asthma were associated with elevated levels of aeroallergens, especially with fungal spores.^{21–24} Fungal spores also provoke hypersensitivity in asthmatics via production of immunoglobulin E (IgE).^{24,39}

In the present study, we investigated the association between selected types of spores and visits to the emergency department for asthma among children under 10 years of age. After accounting for the potential confounding effects of

ambient air pollution and changes in weather, we found that first visits to the emergency department for asthma increased when concentrations of *Basidiomycetes*, *Deuteromycetes*, and *Cladosporium* spores were increased 3 or more days beforehand. For *Basidiomycetes*, there was also a lagged effect for readmissions.

Lewis et al⁴⁰ presented positive findings concerning the effect of *Cladosporium* spores on hospital admissions due to asthma. Other investigators also reported significant positive associations between *Cladosporium* spores and asthma (eg, emergency department visits, peak expiratory flow rates).^{11,22,25,26}

Positive associations between *Basidiomycetes* spores and asthma (eg, hospital admissions, peak expiratory flow rate) have been found^{41,42} and in 2 studies conducted in Canada by Dales and coworkers^{21–23} *Basidiomycetes* spores were found to be associated with emergency department visits as well as hospitalizations. In contrast, other studies showed no associations between *Cladosporium* spores and the exacerbation of asthma^{43–45} nor for *Basidiomycetes* spores.^{32,46,47}

Negative associations were also found in our study between emergency department visits and *Deuteromycetes* spores and *Ganoderma* spores. Significant negative associations between concentrations of *Deuteromycetes* spores and emergency department visits have been also been found by Stieb et al.³² Rosas et al⁴⁸ observed a weak positive association between *Deuteromycetes* and hospital admissions for asthma. A study conducted by Lierl and Hornung⁴⁹ found no association between concentrations of total spores and emergency department visits and hospitalizations for asthma. It is difficult to interpret these negative findings.

Atmospheric pollution may have a confounding effect on the associations between fungal spores and asthma.^{11,17} Dales and coworkers,^{21–23} Delfino et al⁴¹ and Rosas et al⁴⁸ adjusted for a number of atmospheric pollutants (eg, O₃, NO₂, SO₂) and found that they did not greatly influence the associations found between the health indicator data used and concentrations of spores. We also did not find any important confounding effects from concentrations of O₃ and NO₂.

Methodological considerations

Validity of the Health Care Data

Data on visits to the emergency department for asthma were obtained from Quebec's universal health insurance plan where asthma was defined according to the initial assessment of the attending emergency physician. With respect to asthma (ICD9–493) Gdomski et al⁵⁰ showed in a US Medicaid study that code-recoding errors are minimal, although it is unclear whether this is generalizable to data from emergency departments in Montreal. There are no available estimates of the validity or reliability of emergency department visits in Montreal. However, asthma in children can be misdiagnosed and/or confused with other diseases such as bronchitis, and it is likely that in our study there were errors in diagnoses. For example, some admissions coded as asthma may have been

for viral respiratory infections, although viral infections can cause exacerbations of asthma (about 80% to 85% of exacerbations of asthma among children ages 9 to 11 years are from viral).^{43,51,52} Moreover, To et al⁵³ observed that health professionals have a tendency to overdiagnose asthma.⁵⁴ Delfino et al⁵⁵ analyzed Quebec's hospitalization discharge database and showed that the reliability of respiratory diagnoses was higher among young people and that the reliability of diagnoses for asthma was 94.9%. Moreover, infectious agents such as respiratory syncytial virus, which causes bronchiolitis, can lead to the development of asthma among children.¹ In any event, the effects of misclassification, if independent of concentrations of spores, should have led to attenuated estimates of effect.

In recent years in Montreal there has been an effort to control asthma attacks using preventive pharmacological measures (notably combinations of bronchodilators and corticosteroids, taken either preventatively or at time of attack).^{8,56} Indeed, as shown in Table 2 and Figure 4, there has been a decrease over the 11-year study period in emergency department visits for asthma among children, even though the overall incidence has been increasing.

The associations found in this study could be due to chance, to deleterious effects of spores (positive associations), or to a bias introduced by the improved control of asthma following a first visit to the emergency department (negative associations). The significant negative associations observed in the present study, notably those for *Deuteromycetes* spores, with readmissions and total emergency department visits may be due to improved control of asthma following a first visit to the emergency department. After a first visit to the emergency department, patients could receive information from health professionals about their condition, the principles of eliminating irritants from their environment, and the effective use of medication to better control their disease.

In the absence of personal information on exacerbations (eg, daily diaries), emergency department visits represent a sensitive health indicator (in contrast to hospitalizations, for example). The clinical spectrum of respiratory diseases recorded in emergency department visits is likewise more representative than that found in other contexts because severity of respiratory diseases is larger.⁵⁷

Data on Spores

There was only one single, fixed-site to measure concentrations of spores in the study area. It has been shown previously by Ross et al⁵⁸ and by Lewis et al⁴⁰ that a single collector can represent the temporal variation of the distribution of concentrations of spores of a given species over a large area. We used the period April 1 to October 31 to capture all spore production activity during the growing season. We found that concentrations of spores were below the level of detection at the beginning of the spring and at the end of fall, and this was probably due to late or early frosts which are known to limit

the production of spore grains.²¹ The truncation of the spore production season may have affected the statistical power to detect associations, especially for *Deuteromycetes* spores, as the strongest spore productions periods normally occur at the end of summer and in early fall.

Confounding

We adjusted for maximum daily temperature, maximum barometric pressure, and maximal concentrations of tropospheric ozone and nitrogen dioxide. Because of the correlations between pollutants (including SO₂ and CO), adjustment for ozone and nitrogen dioxide were probably sufficient to adjust for the potential confounding effects of air pollution. In any event, there were considerable missing data for fine particles (PM_{2.5}) because the nominal sampling frequency was every sixth day and, thus, we did not include this pollutant in the models. However, NO₂ was reasonably well correlated during the study period with PM_{2.5} ($r = .38$). Although wind and precipitation are known to affect concentrations of aeroallergens,^{22,47,59–61} we did not adjust for these weather factors because of missing data. Lastly, we could not adjust for influenza or other viral epidemics because there are no available data sources. Again, however, it is unlikely that these variables would have confounded the observed associations because viral epidemics are not likely to be correlated with spores, as these epidemics usually occur in the colder months that were not included in the study period.

Prevention

It is probably premature to make causal statements regarding specific association between exacerbations of asthma and exposure to certain types of spores, although it seems plausible that such a connection may exist. In our view, the extent of the data and the consistency of the findings of the acute effects of spores on health are, however, not sufficient to make causal statements. With regards to reducing the production of spores, we are not aware of any means for mitigating concentrations. This is unlike the situation with ragweed, for example, where many municipalities have implemented programs to eliminate it from their geographical limits. As well, for air pollution, in many jurisdictions there are ambient air quality standards and guidelines that are supposed to be used to limit concentrations for a few of the “criteria” pollutants.

In the case of some exposures, indices, such as for air quality or ultraviolet light, are available publicly to provide the population with some information to make personal decisions regarding limiting their own personal exposures. The development of such publicly used indices is a nontrivial exercise and requires strong scientific data and extensive field-testing to determine the effectiveness of the maneuver. We do not believe that we are in a position to develop such indices for spores.

Most physicians and other clinicians are not trained to identify risks from most environmental exposures, except

perhaps ultraviolet light, although there is a slowly growing group of occupational physicians who are being trained to identify occupationally related diseases and to manage risks and the course of these diseases. Notable is the training program of Katja Radon and her collaborators at the Ludwig Maximilian University, Munich. Thus, given the state of our knowledge for spores, it would seem that informing physicians of this risk, in the face of ones that have much less uncertainty (eg, air pollution, radon, environmental tobacco smoke, ultraviolet), seems premature.

Conclusion

In conclusion, we found lagged positive effects between *Cladosporium* and *Basidiospores* and initial emergency department visits. Given that the climate is warming, thereby affecting the growing season and increasing the production of spores,⁶² it is possible that stronger associations may be found in the future.

The authors wish to thank the Division of Clinical Epidemiology of McGill University Health Center, the Climate Change Action Fund (Impacts and Adaptation program, project A-571), the Ouranos Consortium (Consortium on Regional Climatology and Adaptation to Climate Change), the Réseau de Surveillance de la Qualité de l’Air de Montréal (Claude Gagnon), and the Meteorological Service of Canada (Québec region). Dr Goldberg gratefully acknowledges receipt of an Investigator Award from the Canadian Institutes for Health Research.

For comments and further information, address correspondence to Mark Goldberg, PhD, Department of Medicine, Division of Clinical Epidemiology, McGill University Health Centre, 687 Pine Avenue West, R4.29, Montreal, Quebec H3A 1A1, Canada.

E-mail: mark.goldberg@mcgill.ca

References

- Demoly P, Godard P, Bousquet J. Une synthèse sur l’épidémiologie de l’asthme. *Rev Fr Allergol Immunol Clin*. 2005;45:464–475.
- Global Initiative for Asthma (GINA). *Global Strategy for Asthma Management and Prevention*. Bethesda, MD: National Institutes of Health. NIH Publication 02–3659. Available at: <http://www.ginasthma.com/>. Accessed December 12, 2006.
- World Health Organization (WHO). *Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death*. 9th revision, Vol. 1–2. Geneva: WHO; 1977.
- Public Health Agency. *Prévention et prise en charge de l’asthme au Canada, un défi de taille maintenant et à l’avenir*. Rapport du Groupe de travail national sur la lutte contre l’asthme, Santé Canada, Ottawa, Laboratoire de lutte contre la maladie; 2000.
- Brutsche MH, Frey U. Pathogenèse et diagnostic de l’asthme. *Forum Med Suisse*. 2002;19:455–463.
- Asthma Society of Canada. About asthma. Available at: <http://www.pq.poumon.ca/>. Accessed December 12, 2006.
- Héguay L, Garneau M, Goldberg MS, Raphoz M, Guay F, Valois MF. Associations between grass and weed pollen and emergency department visits for asthma among children in Montreal. *Environ Res*. 2008;106:203–211.
- Shapiro GG. The ABCs of asthma, causes, effects and relief. *Discover*. 1998;19:S21–S24.
- Campbell NA, Mathieu R. *Biologie*. 1st ed. Bruxelles: De Boeck; 1995.
- Hobbs C. *Medicinal Mushrooms*. Summertown, TN: Botanica Press; 1995.
- Delfino RJ, Coate BD, Zeiger RS, Seltzer JM, Street DH, Koutrakis P. Daily asthma severity in relation to personal ozone exposure and outdoor fungal spores. *Am J Respir Crit Care Med*. 1996;154:633–641.

12. Burch M, Levetin E. Effects of meteorological conditions on spore plumes. *Int J Biometeorol*. 2002;46:107–117.
13. Horner WE, Helbling A, Salvaggio JE, Lehrer SB. Fungal allergens. *Clin Microbiol Rev*. 1995;8:161–179.
14. Lehrer SB, Aukrust L, Salvaggio JE. Respiratory allergy induced by fungi. *Clin Chest Med*. 1983;4:23–41.
15. Becker A, Bérubé D, Chad Z, et al. Canadian Paediatric Asthma Consensus guidelines, 2003 (updated to December 2004): introduction. *CMAJ*. 2005;173:S12–S14.
16. Bernard SM, Samet JM, Grambsch A, Ebi KL, Romieu I. The potential impacts of climate variability and change on air pollution-related health effects in the United States. *Environ Health Perspect*. 2001;109:199–209.
17. D'amato G, Liccardi G, D'amato M, Cazzola M. Outdoor air pollution, climatic changes and allergic bronchial asthma. *Eur Respir J*. 2002;20:763–776.
18. Oliveira M, Ribeiro H, Abreu I. Annual variation of fungal spores in atmosphere of Porto: 2003. *Ann Agric Environ Med*. 2005;12:309–315.
19. Sabariego S, Diaz De La Guardia C, Alba F. The effect of meteorological factors on the daily variation of airborne fungal spores in Granada (southern Spain). *Int J Biometeorol*. 2000;44:1–5.
20. Sabariego S, Diaz De La Guardia C, Alba F. Estudio aerobiológico de los conidios de alternaria y *Cladosporium* en la atmósfera de la ciudad de Almería (SE de España). *Rev Iberoam Micol*. 2004;21:121–127.
21. Dales RE, Cakmak S, Burnett RT, Judek S, Coates F, Brook JR. Influence of ambient fungal spores on emergency visits for asthma to a regional children's hospital. *Am J Respir Crit Care Med*. 2000;162:2087–2090.
22. Dales RE, Cakmak S, Judek S, et al. The role of fungal spores in thunderstorm. *Asthma Chest*. 2003;123:745–750.
23. Dales RE, Cakmak S, Judek S, et al. Influence of outdoor aeroallergens on hospitalization for asthma in Canada. *J Allergy Clin Immunol*. 2004;113:303–306.
24. Lehrer SB, Hughes JM, Altman LC, et al. Prevalence of basidiomycete allergy in the USA and Europe and its relationship to allergic respiratory symptoms. *Allergy*. 1994;49:460–465.
25. Malling HJ. Diagnosis and immunotherapy of mould allergy. IV. Relation between asthma symptoms, spore counts and diagnostic tests. *Allergy*. 1986;41:342–350.
26. Neas LM, Dockery DW, Burge H, Koutrakis P, Speizer F. Fungus spores, air pollutants, and other determinants of peak expiratory flow rate in children. *Am J Epidemiol*. 1996;143:797–807.
27. Statistics Canada. 2001 census, geocoded data (electronic output). Available at: <http://geodepot.statcan.ca/Diss/index.f.cfm>
28. Eilstein D, Le Tertre A, Zeghnoun A, et al. *Séries temporelles et modèles de régression: Application à l'analyse des associations à court terme entre la pollution atmosphérique et la santé*. Paris: Institut de Veille Sanitaire; 2005.
29. Goldberg MS, Burnett RT, Brook J, Bailar JC, Valois MF, Vincent R. Associations between daily cause-specific mortality and concentrations of ground-level ozone in Montreal, Quebec. *Am J Epidemiol*. 2001;154:817–826.
30. Goldberg MS, Burnett RT, Stieb DM. A review of time-series studies used to evaluate the short-term effects of air pollution on human health. *Rev Environ Health*. 2003;18:269–303.
31. Goldberg MS, Burnett RT, Yale JF, Valois MF, Brook JR. Associations between ambient air pollution and daily mortality among persons with diabetes and cardiovascular disease. *Environ Res*. 2006;100:255–267.
32. Stieb DM, Beveridge RC, Brook JR, et al. Air pollution, aeroallergens and cardiorespiratory emergency department visits in Saint John, Canada. *J Expo Anal Environ Epidemiol*. 2000;10:461–477.
33. Tobias A, Galan I, Banegas JR. Non-linear short-term effects of airborne pollen levels with allergenic capacity on asthma emergency room admissions in Madrid, Spain. *Clin Exp Allergy*. 2004;34:871–878.
34. Chen Y, Yang Q, Krewski D, Burnett RT, Shi Y, McGrail KM. The effect of coarse ambient particulate matter on first, second, and overall hospital admission for respiratory disease among the elderly. *Inhal Toxicol*. 2005;17:649–655.
35. Cao J, Valois MF, Goldberg MS. An S-Plus function to calculate relative risks and adjusted means for regression models using natural splines. *Comput Methods Programs Biomed*. 2006;84:58–62.
36. Goldberg MS, Bailar JC, Burnett RT, et al. Identifying subgroups of the general population that may be susceptible to short-term increases in particulate air pollution: a time-series study in Montreal, Quebec. *Res Rep Health Eff Inst*. 2000;97:7–113.
37. Feinberg SM, Little HT. Mould allergy. Its importance in asthma and hay fever. *Wis Med J*. 1935;34:254–262.
38. Van Leeuwen WS. Bronchial asthma in relation to climate. *Proc R Soc Med*. 1924;17:19–26.
39. Gergen PJ, Turkeltaub PC. The association of individual allergen reactivity with respiratory disease in a national sample: data from the second National Health and Nutrition Examination Survey, 1976–80 (NHANES II). *J Allergy Clin Immunol*. 1992;90:579–588.
40. Lewis SA, Corden JM, Forster GE, Newlands M. Combined effects of aerobiological pollutants, chemical pollutants and meteorological conditions on asthma admissions and A & E attendances in Derbyshire UK, 1993–96. *Clin Exp Allergy*. 2000;30:1724–1732.
41. Delfino RJ, Zeiger RS, Seltzer JM, et al. The effect of outdoor fungal spore concentrations on daily asthma severity. *Environ Health Perspect*. 1997;105:622–635.
42. Hasnain SM, Wilson JD, Newhook FJ. Fungal allergy and respiratory disease. *N Z Med J*. 1985;98:342–346.
43. Carlsen KH, Ørstavik I, Leegaard J, Høeg H. Respiratory virus infections and aeroallergens in acute bronchial asthma. *Arch Dis Child*. 1984;59:310–315.
44. Garty BZ, Kosman K, Ganor E, et al. Emergency room visits of asthmatic children, relation to air pollution, weather, and airborne allergens. *Ann Allergy Asthma Immunol*. 1998;81:563–570.
45. Newhouse CP, Levetin E. Correlation of environmental factors with asthma and rhinitis symptoms in Tulsa, OK. *Ann Allergy Asthma Immunol*. 2004;92:356–366.
46. Epton MJ, Martin IR, Graham P, et al. Climate and aeroallergen levels in asthma: a 12 month prospective study. *Thorax*. 1997;52:528–534.
47. Newson R, Strachan D, Corden J, Millington W. Fungal and other spore counts as predictors of admissions for asthma in the Trent region. *Occup Environ Med*. 2000;57:786–792.
48. Rosas I, McCartney HA, Payne RW, et al. Analysis of the relationships between environmental factors (aeroallergens, air pollution, and weather) and asthma emergency admissions to a hospital in Mexico City. *Allergy*. 1998;53:394–401.
49. Lierl MB, Hornung RW. Relationship of outdoor air quality to paediatric asthma exacerbations. *Ann Allergy Asthma Immunol*. 2003;90:28–33.
50. Gadomski A, Jenkins P, Nichols M. Impact of a Medicaid primary care provider and preventive care on paediatric hospitalization. *Pediatrics*. 1998;101(3):E1.
51. Johnston SL, Pattemore PK, Sanderson G, et al. Community study of role of viral infections in exacerbations of asthma in 9–11 year old children. *BMJ*. 1995;310:1225–1229.
52. Johnston SL, Pattemore PK, Sanderson G, et al. The relationship between upper respiratory infections and hospital admissions for asthma: a time-trend analysis. *Am J Respir Crit Care Med*. 1996;154:654–660.
53. To T, Dell S, Dick PT, et al. Case verification of children with asthma in Ontario. *Pediatr Allergy Immunol*. 2006;17:69–76.
54. Ward DG, Halpin MG, Seamark DA. How accurate is a diagnosis of asthma in a general practice database? A review of patients' notes and questionnaire-reported symptoms. *Br J Gen Pract*. 2004;54:753–758.
55. Delfino RJ, Becklake MR, Hanley JA. Reliability of hospital data for population-based studies of air pollution. *Arch Environ Health*. 1993;48:140–146.
56. Janson S. Action plans in asthma management—why, when, and how? *West J Med*. 1996;165:149–153.
57. Delfino RJ, Murphy-Moulton AM, Becklake MR. Emergency room visits for respiratory illnesses among the elderly in Montreal: association with low level ozone exposure. *Environ Res*. 1998;76:67–77.
58. Ross AM, Corden JM, Fleming DM. The role of oak pollen in hay fever consultations in general practice and the factors influencing patients' decisions to consult. *Br J Gen Pract*. 1996;46:451–455.
59. Anderson W, Prescott GJ, Packham S, Mullins J, Brookes M, Seaton A. Asthma admissions and thunderstorms: a study of pollen, fungal spores, rainfall, and ozone. *Q J Med*. 2001;94:429–433.
60. Caillaud D, Merle P, Marson H, Jeannin A. Tempête et asthme. *Rev Fr Allergol Immunol Clin*. 2005;45:29–32.
61. Packe GE, Ayres JG. Aeroallergen skin sensitivity in patients with severe asthma during a thunderstorm. *Lancet*. 1986;1:850–851.
62. Beggs PJ. Impacts of climate change on aeroallergens: past and future. *Clin Exp Allergy*. 2004;34:1507–1513.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.