The Role of Woodstoves in the Etiology of Nasal Polyposis

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Objective: To determine the role of environmental pollutants in the etiology of nasal polyposis.

Design: Case-control study.

Setting: A community-based hospital practice in the Gaspesian peninsula in rural northeastern Quebec.

Patients: Fifty-five case patients with nasal polyposis and 55 age-matched control subjects without nasal polyposis who were seen at one physician’s practice (J.K.) from March 1, 1998, to December 19, 1998.

Interventions: Exposure to woodstoves, indoor tobacco smoke, and pets and occupational exposures to noxious inhalant compounds.

Results: Forty-five (82%) of the cases, but only 14 (25%) of the controls, reported using woodstoves, yielding a crude odds ratio (OR) of 13.1. The corresponding risk associated with occupational exposure to noxious inhalant compounds was also high (OR, 6.1). When adjusted in various ways for the presence of other factors, these ORs remained high and statistically significant. For woodstove use, the point estimates of the ORs were consistently above 10, with the lower limits of 95% confidence intervals above 5. For occupational exposures to noxious inhalant compounds, the various adjusted OR estimates were above 6, with the lower limits above 1.5.

Conclusions: There is a strong association between the use of woodstoves as a principal source of heating and the development of nasal polyposis. Occupational exposures to noxious inhalant compounds (other than tobacco smoke) also play an important role in its etiology.


NASAL POLYPOSIS is an inflammatory disorder of the nasal mucosa of unknown etiopathogenesis. Several studies have investigated different pathogenic mechanisms. First, there are atopic and nonatopic forms of nasal polyposis. But the atopic form still remains controversial. Eosinophils are the hallmark of the disease. Studies have demonstrated that the cytokine RANTES (regulated on activation, normal T-cell expressed and secreted) is a potent mediator of eosinophil chemotaxis in vitro and of leukocyte recruitment. Other studies assessed the role of interleukins and interferon-γ, cellular adhesion molecule 1, prostanoids, leukotrienes, and u-plasminogen activator. There have been studies that examined the function of T cells infiltrating nasal polyps, the CD8+ (suppressor cell) subpopulation being predominant. The most recent study investigated the relationship between the nitric oxide concentration in the paranasal sinuses and the nasal polyp-derived superoxide anion.

Most studies in the literature have focused on the end point of the inflammatory response. But what triggers this response? The role of infection and inflammation as a cause of nasal polyposis has been widely debated. Ponikau et al studied the role of fungus in the pathogenesis of chronic sinusitis with or without nasal polyposis. They found that the response was non-IgE mediated, with eosinophils as the common denominator. In the study by Morpeth et al., nasal polyps were found in 75% of cases of allergic fungal sinusitis.

The use of woodstoves as a principal source of heating is more prevalent in rural areas, where socioeconomic levels are lower. These stoves liberate high concentrations of suspended particulates of respirable size; (2) gases such as aldehydes, nitrous oxides, carbon monoxide, and sulfur oxides; and (3) polycyclic aromatic hydrocarbons. These noxious inhalant compounds have been known to cause irritation of the mucosa of the upper and lower respiratory tracts, leading to an increased risk of infections. Nitrogen dioxide and polycyclic hydrocarbons...
PATIENTS AND METHODS

From March 1, 1998, to December 19, 1998, a case-control study was conducted in the Gaspesian peninsula in northeastern Quebec. This is a rural community with a population base of approximately 35,000. The population was homogeneous, consisting of only white persons of predominantly Irish and French descent. The prevalence of the acquired immunodeficiency syndrome in the community was extremely low, near 0%. The socioeconomic status was predominantly low and, therefore, an increasing percentage of homes were using woodstoves. One source (Carl Sennett, oral communication, August 2001) estimates the rate at approximately 30% to 40%. In fact, among those who owned a woodstove, most used it as their principal source of heating. The hospital where the patients were examined was in Gaspé (Centre Hospitalier l’Hôtel Dieu de Gaspé). There was only one otolaryngologist (J.K.) serving this community.

CASES

All patients who were referred to the ears, nose, and throat clinic during this period for various ears, nose, and throat complaints were examined by one of us (J.K.). Those who had nasal polyposis were selected for the study. The diagnosis was made on endoscopic examination of the nasal cavity. All cases had unilateral or bilateral disease. None had concurrent cystic fibrosis. A total of 55 cases were identified.

CONTROLS

The 55 controls were randomly selected by one of us (J.K.) based on time available for questioning among the patients who were referred to the same ears, nose, and throat clinic during this period for nonrhinologic complaints. Anyone who had a history of nasal polyposis or recurrent sinusitis or polyps on endoscopic examination was excluded.

EXPOSURES AND OTHER INFORMATION

At the end of the patient visit, the patients were told that one of us (J.K.) was conducting a study on nasal polyposis. After obtaining verbal consent, a standard written questionnaire was administered. The questionnaire inquired about several items, in the following order: (1) telephone number; (2) age; (3) ancestral origin; (4) occupation; (5) exposures to woodstoves, indoor tobacco smoke, pets, and dust; (6) the presence of allergies (hay fever, food, perfume, or aspirin); (7) the presence of associated respiratory illnesses, such as asthma, bronchitis, sinusitis, or otitis; and (8) what season their sinus problems were the most severe. The questions were asked in a standard, orderly, and unbiased fashion. Both groups were unaware of the objective of the study. Cases and controls were similarly distributed geographically and socioeconomically. An additional telephone interview with each subject was conducted by one of us (J.K.) in August 2001 to inquire about the duration and intensity of exposure to woodstoves; these items were not covered in the initial interview.

DATA ANALYSIS

All factors except age were represented as binary variables. The prevalences of each factor in the case and the control (“denominator”) series were calculated, and crude odds ratios (ORs) were calculated. These ORs are used as estimates of relative risk. The degree to which the use of a woodstove tended to co-occur with other factors in the “base” population was assessed by (a) calculating the prevalence of woodstove use among persons in the control series who had these other factors and (b) comparing it with the overall 25% prevalence of woodstove use in all of the controls. We also calculated and report the corresponding prevalences for the case series. We did this so that the raw data showing the association between woodstove use and nasal polyps may be reconstructed separately in those with and without each factor.

As a first level of control for possible confounding of the woodstove–nasal polyps association, we calculated, for each possible confounding factor, an OR that was adjusted for just that factor. We did this by calculating separate ORs for those who did and did not report having the factor. We then calculated a summary OR using the Mantel-Haenszel summary estimator.

We also performed a multiple logistic regression, in which all of these factors were included simultaneously along with the use of woodstoves. Although the average ages of the cases and controls were nearly identical, we included age in all models. We performed the regression analyses again, omitting variables that were not independently associated with nasal polyps and whose exclusion did not materially alter the association of interest. The 95% confidence intervals used throughout indicate the level of precision of our estimates. Confidence intervals that do not include unity indicate that the observed ORs would, in a statistical test, be statistically different from unity at the 5% significance level (2-sided).

The first 3 columns of Table 1 show the characteristics of the 55 cases and the 55 controls. By design, their ages were quite similar (cases: range, 19-88 [median, 50] years; controls: range, 18-80 [median, 48] years). As expected from existing knowledge, there was a male preponderance in cases. Cases were significantly more likely than controls to report a history of allergy, asthma, and aspirin intolerance. We also expected a high prevalence of recurrent si-
The second column of Table 2 shows the ORs when comparisons are restricted to those in whom the various risk factors are absent. For example, in those without allergies, the OR associated with woodstove use is 11.8; in those without asthma, it is 10.7; in those without aspirin intolerance, it is 13.6; and in those without occupational exposures to noxious inhalant compounds, it is 12.9. All of these ORs are similar to the overall OR of 13.1. The numbers of persons with these factors (third column) are smaller and, thus, less stable, but in these persons, the ORs are also still statistically elevated. The last 2 columns of Table 2 give the summary (ie, adjusted) OR estimates, obtained by aggregating the information from the like-with-like comparisons in the first 2 columns. As expected, adjustment just for history of allergy increases the OR from 11.8 to 18.3; for asthma, from 10.7 to 14.1; and for aspirin intolerance, from 13.6 to 14.2. On the other hand, adjustment for occupational exposures to noxious inhalant compounds reduces it slightly from 12.9 to 11.2.

Table 3 shows the raw data and the ORs reflecting the association between nasal polyps and the use of woodstoves in various homogeneous subgroups. Depending on the degree of restriction (absence of factors), the ORs ranged from 10.5 to 15.5, and the lower limits of the confidence intervals were in all instances statistically greater than unity (P<.01 for all, 2-sided).

The first row of Table 4 shows the association between nasal polyps and woodstove use before and after adjustment via logistic regression for all of the other factors or for some of the other factors. The remaining rows of Table 4 show the significant associations with allergy and with occupational exposures to noxious inhalant compounds. As reflected by the fact that the confidence intervals did not include unity, the ORs for woodstove use, allergy, and occupational exposures to noxious inhalant compounds were statistically significant (P<.01), no matter which set of other factors we adjusted for. For aspirin intolerance,
when adjusted for all of the other factors or for some of the factors, the ORs were still elevated but were not statistically significant at the conventional .05 level because the lower limit of the confidence interval was below 1, reflecting the low frequency of this recognized risk factor. Because of the small sample sizes, and as reflected in the generally wide confidence intervals, the magnitudes of the ORs cannot be quantified precisely.

Data on the duration of exposure to woodstoves are as follows: longer than 10 years, 44 (98%) of 45 cases vs 13 (93%) of 14 controls; between 5 and 10 years, 1 (2%) of 45 cases vs 0 controls; and less than 5 years, 0 cases vs 1 (7%) of 14 controls. Data on the intensity of exposure to woodstoves are as follows: longer than 20 hours per day, 15 (33%) of 45 cases vs 0 controls; longer than 14 hours per day, 22 (49%) of 45 cases vs 9 (64%) of 14 controls; and between 6 and 8 hours per day, 8 (18%) of 45 cases vs 5 (36%) of 14 controls. Subjects were exposed in the winter, from November to March. The woodstoves were predominantly (90% [53/59]) located in the basement, where heat can diffuse upward and warm the homes efficiently.

**Table 3. Raw Data and Odds Ratios Measuring the Association Between Nasal Polyps and Woodstove Use in Various Increasingly Homogeneous Subgroups**

<table>
<thead>
<tr>
<th>Woodstove Use</th>
<th>Cases</th>
<th>Controls</th>
<th>Odds Ratio (95% Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-</td>
<td>+/−</td>
<td>20/4 14/33</td>
</tr>
<tr>
<td></td>
<td>+/−</td>
<td>−</td>
<td>38/8 14/40</td>
</tr>
<tr>
<td></td>
<td>+/−</td>
<td>+/−</td>
<td>23/6 11/37</td>
</tr>
<tr>
<td></td>
<td>−</td>
<td>+/−</td>
<td>18/4 14/33</td>
</tr>
<tr>
<td></td>
<td>+/−</td>
<td>−</td>
<td>10/2 11/29</td>
</tr>
<tr>
<td></td>
<td>−</td>
<td>−</td>
<td>19/4 11/36</td>
</tr>
<tr>
<td></td>
<td>−</td>
<td>−</td>
<td>8/2 11/29</td>
</tr>
</tbody>
</table>

*+/− Indicates the presence or absence of the factor; −, the absence of the factor.

**Table 4. Odds Ratio as a Measure of Association of Nasal Polyps With Woodstove Use and Other Factors, Before and After Adjustment by Multiple Logistic Regression**

<table>
<thead>
<tr>
<th>Factor</th>
<th>Adjustment*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
</tr>
<tr>
<td>Woodstove use</td>
<td>13.1 (5.2-32.9)</td>
</tr>
<tr>
<td>Male sex</td>
<td>2.1 (1.0-4.6)</td>
</tr>
<tr>
<td>Allergy</td>
<td>7.6 (3.0-19.0)</td>
</tr>
<tr>
<td>Aspirin Intolerance</td>
<td>10.6 (3.3-30.6)</td>
</tr>
<tr>
<td>Occupational exposures</td>
<td>6.1 (2.4-16.0)</td>
</tr>
<tr>
<td>Tobacco smoke</td>
<td>1.1 (0.5-2.3)</td>
</tr>
<tr>
<td>Pets</td>
<td>0.9 (0.4-2.0)</td>
</tr>
</tbody>
</table>

*Data are given as odds ratio (95% confidence interval). Ellipses indicate data not applicable.

when adjusted for all of the other factors or for some of the factors, the ORs were still elevated but were not statistically significant at the conventional .05 level because the lower limit of the confidence interval was below 1, reflecting the low frequency of this recognized risk factor. Because of the small sample sizes, and as reflected in the generally wide confidence intervals, the magnitudes of the ORs cannot be quantified precisely.

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**COMMENT**

Findings in this study confirm the previously reported associations between nasal polyps, allergy, asthma, and aspirin intolerance. A male preponderance in cases was also consistent with the literature. Two findings are noteworthy. First, there was a remarkably high and statistically significant association between the use of woodstoves as a principal source of heating and nasal polyps. To our knowledge, this is the first report in the literature linking the 2 variables. Second, there was a strong association between occupational exposures to noxious inhalant compounds (other than tobacco smoke) and nasal polyposis. What is common between these 2 findings is that they both involve exposure to noxious inhalant compounds.

The high ORs deserve comment. They can possibly be explained by the high and prolonged exposure to woodstoves. Exposure was substantially higher than in metropolitan areas for several reasons. The available work in this rural community is mainly seasonal, leaving many people unemployed, and at home, in the winter. Given their low socioeconomic level, and the abundance of wood in the area, they tend to heat with wood rather than electricity or oil.

There has been little in the literature regarding the role of noxious environmental pollutants as a possible trigger in the inflammatory response. Pimentel demonstrated in a clinicopathologic study of 92 cases of nasal polyps that environmental pollutants may play a role in their etiopathogenesis. Furthermore, there was a decrease in recurrence when exposure to the offending agent was discontinued. Our study supports Pimentel’s findings of the role of noxious environmental pollutants in the etiopathogenesis of nasal polyposis.
Urea-formaldehyde foam insulation is used extensively for the insulation of buildings. Pross et al.\textsuperscript{22} conducted a study to measure hematological and immunologic variables in subjects with asthma exposed to urea-formaldehyde foam insulation. The main findings were the following: an increase in the eosinophil and basophil count, a slight increase in the T8 (suppressor) cell subpopulation, and a decrease in the natural killer cell response to a low concentration of interferon. Furthermore, the other variables suggest that short-term exposure to formaldehyde may result in some degree of immunosuppression. The acquired immunodeficiency syndrome is a good model to study aberrations in the mean helper/suppressor cell ratio (T4/T8). In patients with the acquired immunodeficiency syndrome, the T4/T8 ratio is severely inverted. However, milder aberrations can be found in patients with other conditions, such as herpes infections, systemic lupus erythematosus with renal disease, burns, and in those who exercise vigorously.\textsuperscript{22}

If, indeed, formaldehyde has caused a mild immunosuppressive state, it would seem plausible that it can lead to an overgrowth of various microorganisms. Yoskovitch and Cantrell\textsuperscript{23} reported the first case of cytomegalovirus associated with nasal polyps in patients with the acquired immunodeficiency syndrome. Sanchez-Segovia et al.\textsuperscript{23} demonstrated a predominance of CD8\textsuperscript{+} suppressor cells in the immunohistochemical analysis of the nasal polyps. Thus, variable degrees of immunosuppression (local and/or systemic) could be the common denominator leading to changes in nitric oxide concentrations in the nasal mucosa, with subsequent overgrowth of microorganisms in certain forms of nasal polyposis. More epidemiological and immunopathologic studies would, therefore, be of interest to examine specifically the relationship of formaldehyde and other noxious environmental pollutants in the development of nasal polyposis. Furthermore, the etiopathogenesis of nasal polyps can be classified into 2 components: (1) internal (immunologic) and (2) external (environmental).

There are some limitations of this study. First, the air-tightness of the woodstoves and homes, reflecting the pollutions in the nasal mucosa, with subsequent overgrowth of microorganisms, with the development of nasal polyps. Thus, variable degrees of immunosuppression (local and/or systemic) could be the common denominator leading to changes in nitric oxide concentrations in the nasal mucosa, with subsequent overgrowth of microorganisms in certain forms of nasal polyposis. More epidemiological and immunopathologic studies would, therefore, be of interest to examine specifically the relationship of formaldehyde and other noxious environmental pollutants in the development of nasal polyposis. Furthermore, the etiopathogenesis of nasal polyposis can be classified into 2 components: (1) internal (immunologic) and (2) external (environmental).

As in any case-control study, there is a possibility of recall bias. However, the fact that patients were only told that it was a “study on nasal polyps,” that it inquired about several agents, and that there was no prior awareness of any associations is likely to have minimized these concerns.

Finally, the fact that one of us (J.K.) was also the one who conducted the interviews could be construed as lack of blinding. However, at the beginning of the study, this author (J.K.) was unaware of any association between woodstoves and nasal polyps. The question being studied was the role of environmental pollutants in the workplace or at home and the development of nasal polyps. Woodstoves were included among the exposures because of the high prevalence of woodstove use in this rural community—much higher than in metropolitan cities. Only near the end of the study did the author (J.K.) recognize a pattern in the responses, making blinding more difficult.

In conclusion, this study found a strong association between the use of woodstoves as a principal source of heating and nasal polyposis. To our knowledge, such an association has not been previously reported. There was also a strong association between occupational exposures to noxious inhalant compounds (other than tobacco smoke) and the development of nasal polyposis. These findings merit further investigation.

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### REFERENCES