Airways hyperresponsiveness and atopy: A comparison of Inuit and Montreal schoolchildren

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B HEMMELGARN, E LOOZEN, S SARALEGUI, S CHATWOOD, P ERNST. Airways hyperresponsiveness and atopy: A comparison of Inuit and Montreal schoolchildren. Can Respir J 1995;2(2):92-96.

OBJECTIVE: To compare the prevalence of exercise induced bronchial hyperresponsiveness in Inuit children with that of children in Montreal, and to identify possible genetic and environmental determinants of the differences observed.
DESIGN: Cross-sectional survey.
SETTING: Salluit, an isolated Inuit community in northern Quebec, and Montreal.
POPULATION STUDIED: All children attending school in Salluit in grades 2 to 6 were eligible to participate. For the Montreal study, 18 schools were selected and from each of these, one class from each of grades 1, 3 and 5 were chosen.
MEASUREMENTS: Data collection for both locations included an exercise challenge test to assess exercise induced bronchial hyperresponsiveness (EIBH), allergy skin testing, a questionnaire for parents regarding details of the home environment as well as the child's history of respiratory symptoms, and collection of dust samples from the bedroom floor and mattress for the presence of house dust mite.
RESULTS: The prevalence of EIBH (defined as a decline of 15% or more between pre-exercise forced expiratory volume in 1 s [FEV_1] and that at 5 or 10 mins postexercise) was 19.5% (23 of 118) among the Inuit children, compared with 8.8% (87 of 989) among the Montreal children. In contrast, only 8.6% of the Inuit children had a positive allergy skin test compared with 34% in Montreal.
CONCLUSIONS: A higher prevalence of EIBH was found in Inuit schoolchildren compared with children of similar age in Montreal, although the prevalence of atopy was considerably lower.

Key Words: *Allergy skin test, Exercise induced bronchoconstriction, House dust mite*

Hyperréactivité bronchique et atopie : Comparaison entre écoliers inuit et écoliers montréalais

OBJECTIF : Comparer la prévalence de l'hyperréactivité bronchique induite par l'exercice (HRBE) chez des enfants inuit et chez des enfants montréalais, et identifier les facteurs génétiques et environnementaux potentiels pouvant expliquer les différences observées.
MODÈLE : Étude transversale.
CONTEXTE : Salluit, une communauté inuit isolée dans le nord québécois, puis Montréal.
POPULATION ÉTUDIÉE : L'ensemble des écoliers de Salluit, de la deuxième à la sixième année pouvaient participer à l'étude. À Montréal, 18 écoles ont été sélectionnées. Dans chaque école, une des classes de première, troisième et cinquième année ont été choisies pour l'étude.
MESURES : La collecte des données aux deux endroits de l'étude comprenait une épreuve d'effort pour évaluer l'HRBE, un test cutané d'allergie, un questionnaire pour les parents portant à la fois sur des éléments de l'environnement domestique et sur les antécédents des symptômes respiratoires chez l'enfant, et une collection d'échantillons de poussière provenant du sol de la chambre à coucher et du matelas pour déceler la présence d'acariens de la poussière.
RÉSULTATS : La prévalence de l'HRBE (définie par une chute de 15 % et plus entre le volume expiratoire maximum/seconde [VEMS] obtenu avant l'exercice et celui obtenu 5 à 10 minutes après l'exercice) était de 19,5 % (23 sur 118) chez les enfants inuit comparativement à 8,8 % (87 sur 989) chez les enfants montréalais. Inversement, seulement 8,6 % des enfants inuit avaient un test cutané d'allergie positif comparativement à 34 % des enfants montréalais.
CONCLUSIONS : La prévalence de l'HRBE était plus élevée chez les enfants inuit que chez les enfants montréalais du même âge. Toutefois, la prévalence d'atopie était nettement plus faible chez les enfants inuit.

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AVAILABLE EVIDENCE SUGGESTS THAT THE PREVALENCE of asthma in children is particularly frequent in certain populations (1-4), while it is speculated to be nonexistent in others, such as the Inuit living in circumpolar regions (5). These studies have explored the role of genetic and environmental factors, including exposure to environmental tobacco smoke both in utero (6-8) and during early childhood (9-11), and the presence of atopy (9,12,13) and sensitivity to house dust mite (14,15), in an attempt to explain the variations in asthma prevalence observed. Unfortunately the methods and the criteria used to diagnose asthma or bronchial hyperresponsiveness and the environmental factors measured often vary among surveys, limiting the comparisons that can be made.

The purpose of this study was to compare the prevalence of exercise induced bronchial hyperresponsiveness in Inuit children with that of children in Montreal. Similar methodology used in the two locations allowed valid comparisons of the two populations to be made, and also enabled an exploration of differences in the distribution of environmental risk factors. This paper focuses on the results obtained from the first of several Inuit communities currently being studied.

PATIENTS AND METHODS

Study subjects: For the Inuit study, eligible subjects were all children in grades 2 to 6, inclusive, attending school in Salluit, Quebec, an isolated Inuit community (population 848) located at 62° north latitude. Residents of the community were made aware of the study through the school and local radio broadcasts, and written consent was obtained from a parent or guardian of each child before enrolment in the study. All written information to parents and guardians was translated into Inuktitut by an experienced translator and, to ensure comprehension and accuracy, these documents were also translated back into their original form by another independent translator.

School lists in Salluit were used to identify 122 children attending school. Of 121 eligible subjects (one child was excluded from the study population due to a chronic health condition) 120 participated in the study, for an overall participation rate of 99%. Two of the 120 children tested did not successfully complete the exercise challenge test; therefore, the final study sample available for analysis was 118.

For the Montreal study, 18 schools were selected on the island of Montreal to represent a broad range of socioeconomic status. From each school one class of each of grades 1, 3 and 5 were selected, for a total of 1274 children. Each child was provided with a letter, a short questionnaire and a consent form to be completed at home by a parent.

Of 1274 children selected in Montreal, 75 (5.9%) did not return the questionnaire and consent form, while a further 130 (10.2%) of the parents refused participation for their children. Forty-two of these parents did, however, complete the questionnaire; therefore, questionnaire data were available for 1111 of the children. Of 1069 children with consent to participate, 23 were sick or absent, 28 of the exercise tests were not acceptable, 28 of the tests were lost, and one child was excluded because of an asthma attack. Thus, the final study sample available for analysis from Montreal was 989.

In the Montreal study there were no differences between participants and nonparticipants as to age of the child, sex or race. Among families who refused permission for their child to participate in testing at school, but who did return the questionnaire, mothers were more likely to be smokers (37.9% versus 18.8%) and fathers less likely to have a history of asthma (3.9% versus 17.2%).

In the Montreal study a subsample of children was chosen for more detailed investigations in their homes. The subsample contained children with a physician's diagnosis of asthma at any time in the past, as determined from the parent questionnaire, and those whose forced expiratory volume in 1 s (FEV_1) fell by 10% or more after the exercise challenge test in the school. For each of these 'cases' the next child on the alphabetical class list of the same sex was chosen as a 'control'.

Ethical approval for both studies was obtained from the Department of Epidemiology and Biostatistics Ethics Committee of McGill University.

Data collection: In groups from both Salluit and Montreal the outcome of interest, exercise induced bronchial hyperresponsiveness (EIBH), was determined using an exercise challenge test. Following the assessment of normal resting spirometric function, children underwent a 6 min free running exercise test in the school gymnasium (16). The level of exercise was assessed by both the distance covered in the 6 min interval and the heart rate achieved at maximal exercise as measured by a pulsemeter. Postexercise spirometry was measured at 5 and 10 mins following exercise. A positive response of EIBH was defined as a decline of 15% or more between pre-exercise FEV_1 and that at 5 or 10 mins postexercise. All spirometry measurements were performed according to standardized methodology as described by the American Thoracic Society (17). Testing procedures for the exercise challenge test were standardized for the two communities, with the same personnel conducting the tests in both locations. No formal assessment of the reliability of the FEV_1 measurements was undertaken.

The presence of atopy was assessed by skin prick tests to common inhaled allergens using methods described by Bernstein (18). This was carried out in all the Salluit children, but only among the subsample of Montreal children chosen for further study at home. Solutions for testing comprised histamine, normal saline, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, mixed grass pollens, tree pollens, ragweed, mixed molds, *Aspergillus*, *Alternaria*, *Cladosporium* and *Penicillium* species, cat epithelium and cockroach (supplied by Omega Laboratories). A drop of each allergen was placed on the child's forearm and the skin was pricked through the droplet. Measurements of the skin wheal were recorded after 15 mins. The development of one or more wheals at least 3 mm or greater than that resulting from the negative control was regarded as a positive skin test indicating atopy. A subject was considered atopic if he or she had at least one positive test.

TABLE 1
Characteristics of study subjects

	Salluit (n=118)	Montreal (n=1111)
Sex		
Male (%)	46.6	49.8
Age		
Mean	10	8.8
Range	7-15	5-13
Mother smoked during pregnancy (%)	67.3	31.2
Current regular smoking		
Mother (%)	69.6	37.2
Father (%)	49.0	44.4

TABLE 2
Prevalence of EIBH and atopy among children in Salluit and Montreal

	Boys		Girls	
	Salluit (n=55)	Montreal (n=497)	Salluit (n=63)	Montreal (n=492)
EIBH* (%)	23.6	7.8	15.9	9.7
Atopy† (%)	11.1	38.9	6.5	30.8

**Exercise induced bronchial hyperresponsiveness (EIBH) defined as a decline of 15% or more between pre exercise forced expiratory volume in 1 s (FEV_1) and that at 5 or 10 mins postexercise; †Atopy defined as a skin wheal with a mean diameter of 3 mm or more in response to at least one of 13 common inhaled allergens*

In Salluit, trained interviewers from the community administered a questionnaire in Inuktitut to a parent or guardian (usually the mother) of each of the study subjects in their homes. The questionnaire had been translated into Inuktitut and back-translated, in the same manner as the other documents discussed above. In Montreal, the questionnaires, in English or French, were distributed and collected through the schools and self-administered by the parents. Questions included details about the home environment, including smoking history of the parents, and the child's history of respiratory symptoms using questions from the ISAAC (19), IUATLD (20) and American Thoracic Society (21) respiratory symptom and asthma questionnaires.

House dust mite samples were collected by a standard procedure (22) from the mattress and bedroom floor for each of the Salluit study subjects and among the subsample of Montreal children chosen for further study at home. Results are expressed as µg of *D pteronyssinus* I/g of sieved dust. A level of 10 µg/g of dust has been associated with acute attacks and increased risk of future asthma (14).

Data analysis: The intent of this paper is to provide descriptive data, consisting principally of percentage prevalence, rather than to test specific hypotheses. For this reason statistical testing has been limited to that comparing the difference between the proportion of EIBH observed in the two populations using the χ^2 test. Eventually a multivariate analysis will be used to identify determinants of EIBH for each of the two populations separately, as well as together, while controlling for potential confounding variables.

Because allergen skin tests and house dust mites were only measured in the chosen subsample of children in the Montreal study, the results from this subsample were extrapolated to the full sample of Montreal children to estimate the prevalence of these two variables and to allow for a comparison with the prevalence obtained among the Salluit children. The rates of allergen skin test positivity and the prevalence of house dust mite concentrations were extrapolated according to the sampling weights from their observed frequency in the comparison group among the subsample visited at home. The observed frequency among children with EIBH or a history of asthma were then directly combined with the extrapolated frequencies to provide frequencies in the complete group studied in the schools.

RESULTS

Characteristics of study subjects and exposure to tobacco smoke are presented in Table 1. The mean age of the Inuit children was 10 years, slightly older than that of the Montreal children. Inuit children were much more likely to be exposed to tobacco smoke, both in utero and currently, than the Montreal children. Over two-thirds of the Inuit children were exposed to tobacco smoke in utero, compared with less than one-third of the Montreal children. The Inuit children were also more likely to have a mother who was a current smoker (69.6%) than were the Montreal children (37.2%), while the percentage of children whose fathers were current smokers was approximately equal for the two populations.

Among the 118 Inuit children who successfully completed the exercise challenge test, the overall prevalence of EIBH was 19.5%. The prevalence was highest among children seven to nine years old (25%) and decreased to 11% in children 13 to 15 years old. As indicated in Table 2, EIBH in the Inuit was more common in boys (13 of 55, 23.6%) than in girls (10 of 63, 15.9%). In Montreal the overall prevalence was 8.8% and was lower in boys (39 of 497, 7.8%) than in girls (48 of 492, 9.7%), though the sex difference in Montreal children was proportionately less than among Inuit children. In a comparison of the two populations, the prevalence of EIBH was significantly higher among the Inuit boys than among the Montreal boys ($P<0.001$), but there was no significant difference in the prevalence of EIBH between Inuit and Montreal girls ($P>0.10$).

Rates of atopy, or allergy skin test positivity, were much lower among the Inuit children. Overall, 8.6% of the Inuit children had a positive skin test compared with 34% of the Montreal children ($P<0.001$). The prevalence of atopy was higher among boys in both the Inuit and Montreal children (Table 2).

The prevalence of the child's respiratory symptoms, as reported by parents, was consistently higher among the Inuit population (Table 3).

House dust mite was virtually nonexistent among the Inuit. Only one of 93 bedroom floor samples and none of the 93 mattress samples contained 1 g or more of total dust mite/g

of dust. The corresponding levels in Montreal, when extrapolated to the full sample, were 15.6% for bedroom floor samples and 23.6% for mattress samples.

DISCUSSION

In a cross-sectional study of 118 Inuit schoolchildren we observed a high prevalence of airways hyperresponsiveness as shown by EIBH. With respect to the influence of age, results of our data are similar to those reported by Bardagi (23), in that the prevalence of EIBH decreased progressively with age. This excess in a measure of bronchial hyperresponsiveness appears to be contrary to the commonly held belief among physicians working with the population that asthma is an unusual occurrence (5). This contradiction may be more apparent than real, however, since the airway hyperresponsiveness may be of a different etiology than that commonly found among children with allergic asthma, and may manifest ifself differently clinically from the asthma we usually recognize among children in more southern climates.

We chose to assess bronchial hyperresponsiveness using an exercise challenge test rather than another bronchoconstrictive stimulus such as histamine or methacholine for two primary reasons. First, the validity of exercise as a means of assessing airway narrowing has been demonstrated (23), and second, exercise was felt to be a more practical and safe stimulus to use in these remote isolated communities than pharmacological induction of airway narrowing. We are not sure whether the excess bronchial hyperresponsiveness observed would also occur with methacholine or histamine. While it has been demonstrated that responses to these different bronchoconstrictive stimuli correlate within individuals, this correlation is inconsistent and relatively weak (24), though exercise induced bronchospasm may be more specific to asthma (25).

Skin test reactivity to common inhaled allergens was present in less than 10% of the Inuit children, compared with a third or more of children in Montreal, suggesting that allergic sensitization was uncommon. Furthermore, the most important allergenic cause of asthma, the dust mite, could not be detected in most bedrooms of Inuit children and was never present at levels thought to be associated with sensitization or acute symptoms (14).

On the other hand, exposure to tobacco smoke was extremely common in the Inuit children due to both a very high prevalence of smoking among parents and the amount of time spent indoors in these northern regions. The relationship between exposure to second-hand smoke and an increase in bronchial responsiveness among children has previously been described (26). Cold air, proposed by some as a cause of airway disease, is another potential irritant that may partially account for the high prevalence of EIBH among the Inuit children (27,28). However, a more likely explanation may be the very high rate of both upper and lower respiratory tract infections occurring among Inuit children during infancy and early childhood. Evidence from the literature suggests that respiratory infections may have long term consequences on airway function (29).

TABLE 3
Prevalence of respiratory symptoms among children in Salluit and Montreal

	Salluit (n=118)	Montreal (n=1111)
Wheezing		
Ever (%)	15.4	10.6
Past 12 months (%)	7.7	3.2
Cough		
Persistent (%)	25.6	10.3
At night (%)	17.1	10.2
With phlegm (%)	31.0	6.5

Meteorological conditions in the gymnasiums where the exercise tests were conducted were similar in the two locations, and therefore were not likely to have influenced the difference in EIBH observed. Average temperature and humidity were 22.0°C and 22.8%, respectively, in Salluit and 19.3°C and 29.8%, respectively, in Montreal.

It would be difficult to attribute the high prevalence of bronchial hyperresponsiveness to social disadvantages alone, since the relationship between bronchial hyperresponsiveness and socioeconomic status has been weak and inconsistent in previous studies (30,31). It is also unlikely that heating methods accounted for the differences observed. All Inuit homes were heated with an oil furnace, while in Montreal the majority of homes used electric radiators. A genetic component may be present since respiratory diseases remain an important cause of mortality and morbidity among adult Inuit, which is evident despite the reduction in prevalence of tuberculosis (32).

Although these results are preliminary and must be interpreted as such, they do suggest that the prevalence of airways hyperresponsiveness, as shown by EIBH, is considerably higher among Inuit school children than among children of similar age in Montreal. However, the presence of atopy is remarkably lower ($P<0.001$). We are currently examining several hundred more Inuit children and will be exploring the potential role of the indoor environment, as well as medical history of respiratory illness, in bringing about this high rate of exercise induced bronchial hyperresponsiveness.

ACKNOWLEDGEMENTS: We thank the Salluit Education and Health Committees, the staff of the Salluit School, and the CPDPM of the Inuulitsivik Health Centre for their support and assistance in carrying out this study. This study was supported by a grant from the National Health Research and Development Program, Health and Welfare Canada, and the Quebec Lung Association. P Ernst is a senior research scholar of the Fonds de la recherche en santé du Québec (FRSQ), and B Hemmelgarn is the recipient of a doctoral scholarship from the National Health and Research Development Program of Canada (NHRDP).

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