

Relative Scarcity of Asthma and Atopy among Rural Adolescents Raised on a Farm

PIERRE ERNST and YVON CORMIER

Unité de Recherche, Centre de Pneumologie, Hôpital Laval, Quebec; and the Respiratory Division, McGill University Health Centre, Montreal, Quebec, Canada

We determined the prevalence of markers of atopy and asthma among 1,199 rural secondary school students ages 12 to 19 yr. Subjects identified as having been raised on a farm and half as many subjects without regular exposure to a farming environment from the same school class completed a respiratory symptom questionnaire and underwent allergy skin tests and a methacholine bronchoprovocation test. Current wheeze, airways hyperresponsiveness (AHR), and skin test positivity to inhaled allergens were all significantly less common among adolescents raised on the farm and these differences were especially pronounced in girls. After adjusting for gender and current smoking, the odds ratios for being raised on a farm were: 0.70 (95% CI 0.52 to 0.95) for current wheeze; 0.59 (95% CI 0.37 to 0.95) for asthma, defined as the concomitant occurrence of wheeze and AHR; and 0.58 (95% CI 0.46 to 0.75) for atopy defined as a positive reaction to any one of 24 common inhaled allergens. These associations were also not significantly altered by adjusting for the difference in the number of siblings.

Asthma and atopy have been increasing in frequency in many parts of the world (1–4). While there has been much speculation (5–7) as to the reasons for these time trends, an adequate explanation remains elusive. Further clues may be obtained by examining genetically homogeneous populations in contrasting environments. Several reports have suggested a lower prevalence of allergic disease, including diagnosed asthma, among young people exposed to a farming environment (8, 9). Studies among older subjects have often reported an excess of these disorders (10, 11). With this in mind we examined adolescents from an ethnically homogeneous area of rural Quebec and compared the frequency of markers of asthma and atopy among those who were raised on a farm to those who, though raised in the same rural area, had not been in regular contact with a farm or farming practices.

Children raised on family farms in Quebec are exposed in early life to environments such as dairy barns, pigsty, and aviaries. Most farm women participate actively in farm chores so that small children are frequently allowed to play in these buildings. Also children actively take part in the farm chores from the age of 7 or 8 yr. Farm buildings contain large quantities of airborne bacteria, endotoxins, fungi, animal danders and proteins, feed dusts, and a variety of chemicals used in these buildings (cleaning products, insecticides, etc.) (10). Children are therefore exposed to large quantities of allergens, toxins, and irritants. We hypothesized that such differences in early childhood exposures between those adolescents raised or not on the farm might be reflected in differences in the prevalence of allergic disease.

METHODS

We approached 14 secondary schools in rural areas surrounding Quebec City where the principal industry is farming, primarily dairy farming, cattle raising, and swine confinement. Of 9,751 names on the school rolls for the academic year, all 9,082 children present the day of the study team's initial visit to the school self-completed the International Study of Asthma and Allergies in Childhood (ISAAC) allergic disease questionnaire (12) to which were added several questions to allow us to detail exposure to the farming environment. We identified all subjects currently living on a farm and then selected from the same school class half the number of subjects, matching for gender, among those who had never lived or worked on a farm in their lifetime. These 1,594 subjects were provided with a letter to their parents requesting approval for their child's participation in the study. A total of 1,340 (84%) granted permission and completed the European Community Respiratory Health Survey (ECRHS) questionnaire (13). The 1,199 subjects who completed all the tests successfully form the basis for the present report. This represents 802 of 1,055 subjects chosen from a farming environment (76%) and 397 of 539 from a nonfarming environment (74%).

The report of wheezing in the last 12 mo (current wheeze) was obtained from the French version of the ECRHS questionnaire. The questionnaire was self-administered but completed at home so that help could be obtained from parents. Information on smoking habits was obtained confidentially by direct questions just prior to allergy and lung function testing. Subjects were considered to be currently smoking if they smoked one or more cigarettes per day at the time of the testing.

Subjects underwent allergy skin tests, spirometry, and methacholine bronchoprovocation at school. Allergy skin tests were carried out by the skin prick test method using a 26-gauge needle to prick through a drop of each allergen as well as a positive (histamine) and negative control (saline) on the volar surface of the forearm. Reactions were read at 15 min by applying a piece of tape to the skin surface and outlining the reaction. The marked tape was transferred to a data sheet and the two largest perpendicular diameters were recorded. A reaction to a specific allergen was considered to be positive if the largest diameter measured at least 3 mm more than the negative control. We chose the following locally relevant common inhaled antigens (Omega, Montreal, Canada): the dust mites, *Dermatophagoides pterynissinus* and *D. farinae*, cat, dog, ragweed, *Alternaria*, *Cladosporium*, tree mixture, maple, birch, oak, weed mixture, grass mixture, *Hormodendrum*, *Alternaria*, *Penicillium*, *Mucor*, *Aspergillus*, *Helminthosporium*, horse, cow, pig, and feathers. In 1,100 subjects we were also able to test for allergic sensitization to the storage mites, *Lepidoglyphus destructor*, *Acarus siro*, and *Tyrophagus putrescentiae* found in barns, using allergens graciously supplied by ALK (Copenhagen, Denmark). Subjects were considered to be atopic if they had a positive reaction to any one of the allergens used. Domestic atopy was defined as a positive reaction to at least one of cat, dog, *D. pterynissinus* or *D. farinae*. Farm allergy was defined as a positive reaction to one of horse, cow, pig, and three storage mites without any positive reactions to the common inhaled allergens also tested for.

Spirometry was carried out sitting with the subject wearing a nose clip. Acceptability of results was judged according to American Thoracic Society recommendations (14). Methacholine was administered by individually calibrated DeVilbiss number 40 nebulizers (DeVilbiss, Willow Grove, PA) according to the protocol described by Yan and colleagues (15). Airways hyperresponsiveness (AHR) was considered to be present if the FEV₁ dropped by 15% or more at the highest concentration administered.

(Received in original form August 27, 1999 and in revised form November 11, 1999)

Supported by Health Canada, NHRDP Grant 6605-4369-502 and the Respiratory Health Network of Centres of Excellence.

Correspondence and requests for reprints should be addressed to Dr. Pierre Ernst, M.D., Clinical Epidemiology, Royal Victoria Hospital, 687 Pine Avenue West, R4.29, Montreal, PQ, H3A 1A1 Canada. E-mail: pierre.ernst@clinepi.mcgill.ca

Am J Respir Crit Care Med Vol 161. pp 1563–1566, 2000

Internet address: www.atsjournals.org

A subject was considered to have "asthma" if he demonstrated AHR on methacholine testing and reported the occurrence of wheeze in the last 12 mo (16).

Prevalence of the outcomes of interest were compared using the chi-square statistic and multiple logistic regression was used to compare the odds ratios of being raised on a farm given the occurrence of the outcomes examined after adjusting for gender, current smoking, and number of siblings. All analyses were carried out using SAS (SAS Institute Inc., Cary, NC).

RESULTS

To contrast those children with and without exposure to the farm environment, we eliminated from consideration all those who had been exposed, either previously or intermittently to farming practices either by having worked or lived on a farm. To assure that these subjects (referred to as others in Table 1) did not represent a group of adolescents who had been selected away from farm exposures for health reasons or due to susceptibility to allergenic exposures, we compared their responses to the ISAAC questionnaire to that of the subjects without any farm exposure (nonfarm) and who were therefore eligible to be selected as part of the comparison group for the study proper. The prevalence of wheeze ever, current or with exercise, diagnosed asthma, rhinitis, and eczema was very similar in the two groups, suggesting that there had not been significant drifting away from the farm environment of symptomatic or susceptible children.

Of the 1,199 adolescents who completed all the tests properly, there were 564 boys and 635 girls. As seen in Table 2, the report of wheeze in the last 12 mo, the presence of AHR, and the combination of the two, used to define asthma, were significantly less common among adolescents raised on the farm. This was also true for skin test positivity to common inhaled allergens, our definition of atopy, though not when skin test positivity to farm allergens alone was considered. These differences were most marked among girls, so that, when boys were considered separately, none of the differences between boys raised or not on the farm achieved statistical significance. Girls were more often current smokers than boys (20% as compared with 10.6%), while overall those raised on a farm smoked much less often (12.7% as compared with 21.4%). The FEV₁/FVC did not differ between those raised or not in a farming environment (mean of 0.88 and standard deviation of 0.056 in both groups).

The presence of domestic pets was very common among subjects on the farm. Those on the farm reported the presence of cats in 76% of cases as compared with 36% for those not living on a farm. Dog ownership was reported by 71% of those on the farm and 45% of those not on the farm. Despite the more frequent presence of pets on farms, cats and dogs were less frequently allowed in the bedroom; 20% of farm children

reported the presence of a cat in the bedroom as compared with 29% not on the farm ($p = 0.001$). For the presence of dogs in the bedroom the prevalence was 21% for farm children and 27% for nonfarm subjects ($p = 0.01$). Interestingly, allergic sensitization to household pets was twice as prevalent among subjects not raised on a farm; a positive allergy skin test to cat allergen was present in 16% of nonfarm children and 8% of subjects exposed to the farm environment. For sensitization to dog allergen the prevalence was 9% and 4% in the nonfarm and farm children respectively. There was no difference in the frequency of allergy in their parents as reported by the children on the ECRHS questionnaire. Allergic disease in the father was reported by 18% of exposed as compared with 19% of nonexposed subjects. For the report of allergic disease in the mother the prevalence was 29% and 30%, respectively.

We used logistic regression to adjust for the possible modifying effects of gender and the differences in the prevalence of smoking in order to examine the independent association between the outcomes of interest and being raised on a farm. As demonstrated in Table 3, those with wheeze, asthma, and atopy were significantly less likely to come from a farming environment. We further adjusted for the number of siblings, because family size was significantly greater in those living on a farm (2.45 versus 1.67 siblings; $p = 0.0001$). A protective effect of the farming environment against wheeze, AHR, asthma, and atopy persisted. Because of the importance of indoor allergens, we also redefined atopy with the requirement that a subject, to be considered atopic, should have a positive skin test to at least one of cat, dog, *D. pterynissinus*, or *D. farinae*. Use of this definition of atopy did not modify the association

TABLE 1
SYMPTOMS AND ALLERGIC CONDITIONS IN THE
TARGET POPULATION AS REPORTED ON THE
ISAAC QUESTIONNAIRE

	Farm	Nonfarm	Others
n*	1,034	5,981	2,067
Wheeze ever, %	20.9	25.8	26.7
Current wheeze, %	12.7	17.2	17.7
Exercise wheeze, %	18.4	23.9	24.5
Asthma ever, %	5.8	8.3	8.6
Rhinitis ever, %	30.2	35.0	36.2
Eczema ever, %	11.3	12.1	10.9

* Only subjects who responded to all of the items in the table are included.

TABLE 2
MARKERS OF ASTHMA AND ALLERGY AMONG ADOLESCENTS
RAISED OR NOT RAISED ON THE FARM (n = 1,199)

	Farm (n = 802)	Nonfarm (n = 397)	p Value
Wheeze* %			
All	17.1	24.7	0.002
Boys	14.9	19.1	0.22
Girls	19.2	28.8	0.005
AHR† %			
All	12.9	17.4	0.035
Boys	11.1	14.9	0.21
Girls	14.6	19.2	0.12
Asthma‡			
All	5.1	9.3	0.005
Boys	4.3	6.6	0.26
Girls	5.9	11.4	0.01
Atopy§			
All	40.8	53.4	0.001
Boys	46.0	53.6	0.10
Girls	35.7	53.3	0.001
Farm allergy			
All	5.7	3.8	> 0.05
Boys	6.3	3.1	> 0.05
Girls	5.2	4.4	> 0.05
Current smoking¶ %			
All	12.7	21.4	0.001
Boys	8.6	15.5	0.02
Girls	16.8	25.8	0.006

* Wheeze is the report of wheeze in the last 12 mo on the ECRHS questionnaire.

† AHR: 15% or greater drop in FEV₁ with methacholine.

‡ Asthma: presence of both wheeze and AHR.

§ Atopy is a 3-mm or larger skin wheal to any one of 24 inhaled allergens.

|| Farm allergy is defined as a positive reaction to one or more farm allergens alone (horse, cow, pig, and three storage mites). Testing for storage mites was not available for 99 subjects (n = 1,100).

¶ Current smoking is the report of smoking one or more cigarettes per day at the time of testing.

TABLE 3
CRUDE AND ADJUSTED ODDS RATIOS FOR THE RELATION BETWEEN VARIOUS MARKERS
OF ASTHMA AND ALLERGY AND BEING RAISED ON A FARM (n = 1,199)

Outcomes*	OR Crude (95% CI)	OR Adjusted [†] (95% CI)	OR Adjusted [‡] (95% CI)
Wheeze	0.63 (0.47–0.84)	0.70 (0.52–0.95)	0.72 (0.56–0.99)
AHR	0.70 (0.50–0.98)	0.76 (0.55–1.07)	0.80 (0.56–0.87)
Asthma	0.52 (0.33–0.83)	0.59 (0.37–0.95)	0.71 (0.37–0.98)
Atopy	0.60 (0.47–0.77)	0.58 (0.46–0.75)	0.62 (0.48–0.80)

Definition of abbreviations: CI = confidence interval; OR = odds ratio.

* See legend to Table 2 for definitions.

[†] OR are adjusted for gender and current smoking.

[‡] OR are adjusted for gender, current smoking, and number of siblings.

with living on a farm; odds ratio of 0.59 with a confidence interval of 0.46 to 0.76, unadjusted or after accounting for gender, current smoking, and number of siblings.

DISCUSSION

We have found a significantly lower prevalence of asthma, defined as current wheeze and AHR to methacholine and atopy, as attested to by a positive immediate skin test response to one of 24 common inhaled allergens, in children raised on the farm as compared with children attending the same schools in the same rural areas but who had not been subjected to regular contact with the farm environment. These differences were especially pronounced among girls and were not explained by differences in current smoking or family size. There was no difference in the prevalence of airflow limitation between the groups as assessed by spirometry.

This relative deficit of asthma and related syndromes might have resulted if families with symptomatic children were more likely to have left the farm in order to remove their children from further exposure. We examined this possibility by comparing the prevalence of wheeze, reported asthma, allergic rhinitis, and eczema, as determined with the ISAAC questionnaire used at screening, between subjects without significant exposure to a farming environment, among whom the comparison group was randomly chosen, and subjects with past or intermittent exposure to farming. No excess of allergic disease was found among this latter group which includes subjects having left a farming environment during childhood, thus making it unlikely that an exodus of affected individuals could explain the lower prevalence of asthma syndromes among those raised on a farm and still currently living there.

The inclusion of all subjects attending school on the day of testing and further testing of 84% of these subjects makes selection bias an unlikely explanation for our results. Furthermore, response rates were similar for those raised or not on the farm and the prevalence of allergic disease as attested to by responses to the ISAAC questionnaire was not different among adolescents who did not participate in further testing. More girls than boys were enrolled in school, raising the possibility that boys not in school may have been more likely to be working on the farm. This may have caused an underestimation of the true differences between boys raised or not in a farming environment because it seems likely that it would be those boys without health problems who would have left school early to work.

The health outcomes chosen are those in common use in epidemiological studies of respiratory and allergic disease, and the methods of measurement chosen are well described and standardized. The definition of asthma used, the concomitant report of wheeze and nonspecific airways responsiveness, has been proposed as particularly appropriate for use in epidemiological studies (16).

Atopy was defined as a positive reaction to any one of 24 inhaled allergens and would be expected to be a sensitive measure of an atopic tendency.

Smoking was much less prevalent among adolescents living on the farm. This might provide a partial explanation for the lower prevalence of AHR among adolescents raised on the farm. It is noteworthy in this respect that the inverse relationship between AHR and living on a farm was reduced when differences in the prevalence of smoking were accounted for. Differences in smoking habits did not explain the lower prevalence of allergy skin positivity among those raised on the farm. Of interest, the prevalence of sensitization to farm allergens alone was not lower among adolescents who had been raised on the farm, attesting to the capability of these subjects to mount an immediate type immune reaction. This raises the possibility that farm allergens may be less relevant to asthma than more common aeroallergens. Requiring the definition of atopy to include sensitization to a common domestic allergen did not affect the inverse relationship between the presence of atopy and being raised on a farm. This resulted because most atopic subjects were positive to at least one of cat, dog, or dust mites. Exposure to domestic pets differed according to the living environment. While the presence of domestic pets was more common on the farm, subjects living on the farm were less likely to allow the animal into the bedroom. One can speculate that exposure to pet allergen may be much higher in children not raised on the farm which might be, in part, responsible for the higher frequency of sensitization to pets among nonfarm children.

The most likely explanation for our results is that exposure to the varied and complicated blend of irritant, allergenic, and infectious factors and agents in early childhood somehow favors the development of tolerance to the allergenic properties of common inhaled aeroallergens and the bronchial hyperresponsiveness which is commonly associated with allergic sensitization. It may be that exposure to the farming environment, perhaps by promoting T helper cell, type 1 (Th1) as opposed to Th2 type immunological responses early in life (17), reduces the likelihood of developing asthma and atopic disease. Similar deficits in allergic disease have been described in relation to various aspects of early childhood experience such as air pollution (18), the use of various heating fuels (19), a westernized life style (20) and early exposure to infectious agents (21, 22). Farming families have more children and increasing family size has been associated with a reduction in the prevalence of allergic disease (23–25). The differences in the number of siblings between farming and nonfarming families did not account for the differences in the prevalence of asthma and atopy in our results, however. We have no information on diet and it is possible that differences in the consumption of certain foods, especially fresh fruits and vegetables (6, 26), might explain the differences observed. This seems unlikely because all study subjects were living in the same rural envi-

ronment and were attending the same schools. A less likely explanation for our results is health selection across generations. Selection of subjects and families with a lower propensity to allergic disease into farming could possibly have occurred. This would not explain the more pronounced differences seen among girls, however. Furthermore, because of the rural and close-knit nature of the communities studied, most of the children selected in the nonfarm group are likely to have had a parent or grandparent who was raised on a farm, leaving at the most a very short time in terms of generations for such a selective process to occur. Furthermore, the crude evaluation of parental allergy obtained by questionnaire from the children gave no evidence of a difference in allergic disease in the parents of subjects raised or not on a farm.

Our results are similar to and complement those from a large population-based study in Switzerland (8). Braun-Fahrlander and coworkers found lower rates of allergic disease as reported by questionnaire and a lower likelihood of demonstrating a positive specific IgE antibody to common inhaled allergens, especially those commonly found indoors, among children whose parental occupation was farming. They did not have objective evidence to support the diagnosis of asthma, however.

Our results have implications for studies of hazards of farming that have an allergenic mechanism and/or target the airways. In light of the lower prevalence of allergy and asthma among adolescents raised on the farm and the likelihood that adult farmers will tend to be recruited from this population group, any cross-sectional study of allergic or airway disease among adult farmers will significantly underestimate the true risk of such hazards. This is especially pertinent given the report of farming as the most consistent risk factor for occupationally related asthma in the ECRHS (11).

Acknowledgment: The authors are grateful for the careful attention to data gathering provided by Martine Poulin, R.N., and Marie Blouin, R.N., and for the help with data handling and analysis provided by Serge Simard, Bing Cai, and Ye Hua.

References

- Manfreda, J., A. B. Becker, P. Z. Wang, L. L. Roos, and N. R. Anthonisen. 1993. Trends in physician-diagnosed asthma prevalence in Manitoba between 1980 and 1990. *Chest* 103:151–157.
- Omran, M., and G. Russell. 1996. Continuing increase in respiratory symptoms and atopy in Aberdeen schoolchildren. *Br. Med. J.* 312:34.
- Aberg, N., B. Hesselmar, B. Aberg, and B. Eriksson. 1995. Increase of asthma, allergic rhinitis and eczema in Swedish schoolchildren between 1979 and 1991 [see Comments]. *Clin. Exp. Allergy* 25:815–819.
- Burr, M. L., B. K. Butland, S. King, and E. Vaughan-Williams. 1989. Changes in asthma prevalence: two surveys 15 years apart. *Arch. Dis. Childhood* 64:1452–1456.
- Bjorkstén, B. 1997. Environmental issues in childhood asthma. *Eur. Respir. Rev.* 7:11–14.
- Seaton, A., D. J. Godden, and K. Brown. 1994. Increase in asthma: a more toxic environment or a more susceptible population? *Thorax* 49:171–174.
- Helms, P. J., and G. Christie. 1999. Prospects for preventing asthma. *Arch. Dis. Childhood* 80:401–405.
- Braun-Fahrlander, C., M. Gassner, L. Grize, U. Neu, F. H. Sennhauser, H. S. Varonier, J. C. Vuille, and B. Wuthrich. 1999. Prevalence of hay fever and allergic sensitization in farmer's children and their peers living in the same rural community-SCARPOL Team. Swiss Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution. *Clin. Exp. Allergy* 29:28–34.
- Aberg, N. 1989. Asthma and allergic rhinitis in Swedish conscripts. *Clin. Exp. Allergy* 19:59–63.
- American Thoracic Society. 1998. Respiratory health hazards in agriculture. *Am. J. Respir. Crit. Care Med.* 158:S1–S76.
- Kogevinas, M., J. M. Anto, J. Sunyer, A. Tobias, H. Kromhout, and P. Burney. 1999. Occupational asthma in Europe and other industrialised areas: a population-based study. European Community Respiratory Health Survey Study Group. *Lancet* 353:1750–1754.
- Asher, M. I., U. Keil, H. R. Anderson, R. Beasley, J. Crane, F. Martinez, E. A. Mitchell, N. Pearce, B. Sibbald, and A. W. Stewart. 1995. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur. Respir. J.* 8:483–491.
- Burney, P. G., C. Luczynska, S. Chinn, and D. Jarvis. 1994. The European Community Respiratory Health Survey. *Eur. Respir. J.* 7:954–960.
- American Thoracic Society. 1987. Standardization of spirometry—1987 update: statement of the American Thoracic Society. *Am. Rev. Respir. Dis.* 136:1285–1298.
- Yan, K., C. Salome, and A. J. Woolcock. 1983. Rapid method for measurement of bronchial responsiveness. *Thorax* 38:760–765.
- Toelle, B. G., J. K. Peat, C. M. Salome, C. M. Mellis, and A. J. Woolcock. 1992. Toward a definition of asthma for epidemiology. *Am. Rev. Respir. Dis.* 146:633–637.
- Holt, P. G., and P. D. Sly. 1997. Allergic respiratory disease: strategic targets for primary prevention during childhood [Editorial] [see Comments]. *Thorax* 52:1–4.
- von Mutius, E., F. D. Martinez, C. Fritzsche, T. Nicolai, G. Roell, and H. H. Thiemann. 1994. Prevalence of asthma and atopy in two areas of West and East Germany. *Am. J. Respir. Crit. Care Med.* 149:358–364.
- von Mutius, E., S. Illi, T. Nicolai, and F. D. Martinez. 1996. Relation of indoor heating with asthma, allergic sensitisation, and bronchial responsiveness: survey of children in south Bavaria. *Br. Med. J.* 312:1448–1450.
- von Mutius, E., S. K. Weiland, C. Fritzsche, H. Duhme, and U. Keil. 1998. Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany. *Lancet* 351:862–866.
- Shaheen, S. O., P. Aaby, A. J. Hall, D. J. Barker, C. B. Heyes, A. W. Shiell, and A. Goudiaby. 1996. Measles and atopy in Guinea-Bissau. *Lancet* 347:1792–1796.
- Shirakawa, T., T. Enomoto, S. Shimazu, and J. M. Hopkin. 1997. The inverse association between tuberculin responses and atopic disorder [see Comments]. *Science* 275:77–79.
- Strachan, D. P. 1989. Hay fever, hygiene, and household size. *Br. Med. J.* 299:1259–1260.
- von Mutius, E., F. D. Martinez, C. Fritzsche, T. Nicolai, P. Reitmeir, and H. H. Thiemann. 1994. Skin test reactivity and number of siblings [see Comments]. *Br. Med. J.* 308:692–695.
- Svanes, C., D. Jarvis, S. Chinn, and P. Burney. 1999. Childhood environment and adult atopy: results from the European Community Respiratory Health Survey. *J. Allergy Clin. Immunol.* 103:415–420.
- Butland, B. K., D. P. Strachan, and H. R. Anderson. 1999. Fresh fruit intake and asthma symptoms in young British adults: confounding or effect modification by smoking? *Eur. Respir. J.* 13:744–750.