Atopy: a predisposing factor for chronic bronchitis in Finland

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Abstract

Study objective – To investigate the predictive value of atopy, smoking, and living in a farm environment in the development of chronic bronchitis.

Design – This was a cross sectional and longitudinal study.

Setting – Postal surveys carried out in Finland in 1975 and 1981.

Participants – The study was part of the Finnish twin cohort study, which included adult twin pairs born in Finland before 1958. The cross sectional sample consisted of 18 351 subjects, including 1025 prevalent cases, and the follow up sample comprised 17 134 subjects, 553 of whom were incident cases of chronic bronchitis.

Main results – According to the cross sectional data, chronic bronchitis was associated with atopy (relative risk 1.41) and smoking (2.43). In the follow up data, chronic bronchitis was related to atopy (1.28), smoking (2.31), and farming (1.45). **Conclusions** – The results confirm the earlier finding in the Finnish farming population that, in addition to smoking, atopy predisposes the development of chronic bronchitis. A farm environment was also found to be a predisposing factor. The results give further support to the “Dutch hypothesis” on the aetiology of chronic bronchitis, according to which atopy is a predisposing factor.

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Classic British studies by Fletcher *et al*¹ showed that chronic bronchitis can be divided into two major types – hypersecretory (simple) and obstructive chronic bronchitis – and that the major determinant in the development of both types was smoking. Atopy did not seem to play any part. Numerous other studies have confirmed the central role of smoking in the pathogenesis of chronic bronchitis. This model of the aetiology of chronic bronchitis was named by Fletcher *et al*¹ the “British hypothesis”. On the other hand, according to Dutch researchers,² chronic bronchitis and asthma represent two aspects of the same underlying mechanisms. Both diseases share common background determinants – an allergic constitution (atopy) and bronchial hyper-responsiveness. Fletcher *et al* termed this theory on the aetiology of chronic bronchitis the “Dutch hypothesis”.¹

Some years ago analyses based on both cross sectional and longitudinal studies among Finn-

ish farmers showed that atopy, irrespective of whether it was defined according to the symptoms or to skin prick test results, predisposed to chronic bronchitis.³ Furthermore, atopy and smoking seemed to have an independent and additive effect on both the prevalence and incidence of chronic bronchitis. These findings were later confirmed in a subsample of the same population, by interview and checking data from the records at the local centres.⁴

We have now analysed the relation between atopy, smoking, and farming and chronic bronchitis in another population consisting of both farming and non-farming groups. We found that atopy predisposed to chronic bronchitis in both groups of individuals giving further support to the Dutch hypothesis.

Subjects and methods

The Finnish twin cohort includes adult twin pairs born in Finland before 1958. Postal questionnaire studies of these twins were carried out in 1975 and 1981. The questionnaires included a diagnostic scale for chronic bronchitis.⁵ Respondents were also asked whether a diagnosis of bronchial asthma, allergic rhinitis, or allergic dermatitis had been made by a doctor. Information on smoking, occupation, and working status was also sought.

The response rate for the 1975 questionnaire study (consisting of several mailing rounds) was 89%, yielding 26 556 responses. People with unknown working status ($n=167$) and those who were not working ($n=7\,410$; consisting of the unemployed or those who had retired due to old age or sickness) were excluded. Of the 18 979 working persons, 17 761 did not have chronic bronchitis and asthma, 1030 reported symptoms of chronic bronchitis, and 188 had asthma or missing data on questions about symptoms of chronic bronchitis. These 188 were excluded. Thus, 18 791 people remained for the cross sectional analyses, and 17 761 persons for the prospective follow up study of chronic bronchitis. After excluding subjects with missing data on smoking or atopy (3.5%), the cross sectional sample comprised 18 351 subjects, including 1025 prevalent cases, and the follow up sample consisted of 17 134 subjects, including 553 incident cases.

Chronic bronchitis and bronchial asthma were measured with the same scales in 1975 and 1981 questionnaires. Where questionnaire data were missing, records on chronic bronchitis from the computerised nationwide hospital discharge register and cause of death records from the death register were linked (from 1 October 1975 to 31 December 1981).

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The data for the incidence of chronic bronchitis were missing in 1.1% (n = 200).

The incidence of chronic bronchitis was analysed in respect of occupational group, contrasting farmers (n = 1855) and other occupations (n = 15 279) by logistic models expressed as relative risks. The 95% confidence intervals were calculated for relative risk (RR) using the formula: $RR = \exp(B \pm 1.96 SE[B])$. The effect of sex, age, history of atopy, and smoking status were adjusted.

The follow up sample (n = 17 134) consisted of 9221 men and 7913 women. The subjects were divided in seven age groups: 18–19y (n = 955), 20–29y (n = 6512), 30–39y (n = 4509), 40–49y (n = 2992), 50–59y (n = 1627), 60–69y (n = 476), and 70 + y (n = 63). There were (according to the 1975 study) 8301 non-smokers or occasional smokers, 3023 ex-smokers, and 5810 current smokers, as well as 2597 subjects with atopy in this sample.

DEFINITIONS

Chronic bronchitis

The respondent was classified as having chronic bronchitis if he or she had coughed up phlegm on most days for at least three months annually. Subjects who fulfilled the criteria of chronic bronchitis but had answered "yes" to the question about asthma diagnosed by a doctor were classified having asthma and were excluded.

Atopy

The respondent was classified as atopic if he or she ever had suffered from allergic rhinitis or allergic dermatitis diagnosed by a doctor.

Smoking

The respondent was classified as a non-smoker if he or she had smoked less than 100 cigarettes ever (or the equivalent in another tobacco prod-

Table 2 Relative risk of chronic bronchitis in relation to age, sex, smoking status, history of atopy and farming occupation among 17 134 subjects according to the follow up study in 1981. Number of subjects is shown in the parenthesis.

	Relative risk*	(95% confidence interval)
Age in 1975 (y):		
18–19 (955)	1.00	
20–29 (6512)	0.23	(0.77, 1.97)
30–39 (4509)	1.69	(1.05, 2.71)
40–49 (2992)	2.10	(1.29, 3.40)
50–59 (1627)	2.54	(1.53, 4.22)
60–69 (476)	2.92	(1.59, 5.38)
70 + (63)	5.49	(2.08, 14.5)
Sex in 1975:		
Male (9221)	1.00	
Female (7913)	0.97	(0.81, 1.7)
Atopy in 1975:		
No (14 573)	1.00	
Yes (2597)	1.28	(1.02, 1.59)
Smoking status in 1975:		
Non-smoker (8301)	1.00	
Ex-smoker (3023)	1.13	(0.86, 1.49)
Current smoker (5810)	2.31	(1.89, 2.82)
Occupation in 1975:		
Non-farmer (15 279)	1.00	
Farmer (1855)	1.45	1.12, 1.87)

* A multiple logistic regression model with 553 incident cases during a six year follow up. Asthmatic, unemployed and retired subjects were excluded.

uct). Those who had smoked more but never smoked daily were classified as occasional smokers and were combined with non-smokers. Those smokers who had stopped daily smoking were classified as ex-smokers. Daily smokers were classified as current smokers.

Results

The prevalence of chronic bronchitis was associated with atopy and smoking (table 1). With regard to the incidence data, chronic bronchitis was significantly related to atopy, smoking, and farming (table 2).

The results were also analysed in a sample that randomly excluded all the other co-twins from complete twin pairs. Those results did not differ from the results based on the sample including twin pairs.

Discussion

The population of the Finnish Twin Registry was chosen as the target of the analysis for three reasons: (1) it is large enough to ensure the analysis has enough power, (2) the two postal surveys made possible the longitudinal approach, and (3) the whole spectrum of occupations was represented in the population. The possible bias due to the genetic concordance was excluded by the analysis of the sample where all the other co-twins were excluded from the complete twin pairs. This analysis yielded results similar to those from the analysis of the whole population.

The diagnosis of chronic bronchitis was based on symptoms, and the questions were designed according to the 1966 version of the MRC questionnaire for respiratory symptoms.⁶ The algorithm for chronic bronchitis met the recommendations of the MRC, and the diagnosis thus obtained meets closely the criteria for chronic bronchitis approved by WHO⁷ and

Table 1 Relative risk of chronic bronchitis in relation to age, sex, smoking status, history of atopy, and farming occupation among 18 351 subjects according to the cross sectional study in 1975. Number of subjects is shown in parenthesis

	Relative risk*	(95% confidence interval)
Age (y):		
18–19 (1011)	1.00	
20–29 (6885)	0.96	(0.71, 1.31)
30–39 (4881)	1.15	(0.85, 1.57)
40–49 (3237)	1.36	(0.99, 1.87)
50–59 (1795)	1.71	(1.22, 2.39)
60–69 (536)	1.75	(1.13, 2.72)
70 + (76)	2.10	(0.86, 5.13)
Sex:		
Male (9904)	1.00	
Female (8447)	1.05	(0.92, 1.21)
Atopy:		
No (15 508)	1.00	
Yes (2843)	1.41	(1.20, 1.65)
Smoking status:		
Non-smoker (8735)	1.00	
Ex-smoker (3212)	1.27	(1.04, 1.55)
Current smoker (6404)	2.43	(2.10, 2.82)
Occupation:		
Non-farmer (16 328)	1.00	
Farmer (2023)	1.11	(0.90, 1.37)

* A multiple logistic regression model with 1025 prevalent cases. Asthmatic, unemployed and retired subjects were excluded.

American Thoracic Society.⁸ The only exception is that the MRC 1966 questionnaire does not ask whether the chronic cough and phlegm have occurred for at least two consecutive years. The reason for this is that British studies have shown that most of those who had cough and phlegm on most days for three months annually had also answered that this had occurred for more than two years.

Chronic cough and phlegm production are also characteristic symptoms of bronchial asthma. Because of this, subjects who answered "yes" to the item on asthma were excluded from the group who otherwise fulfilled the criteria for chronic bronchitis. The hallmark in the diagnosis of clinical asthma is the demonstration of reversible airway obstruction. Although many asthmatics, especially children and young adults, are atopic, atopy *per se* is not included in the diagnostic criteria. The difference observed in the association between atopy and chronic bronchitis in British studies and our study could be explained if atopy were diagnostic criterion for asthma in Britain but not in Finland. This is not, however, a plausible explanation. Moreover, if there has been any diagnostic transfer, it is the other way, from chronic bronchitis to asthma. The reason for this is that in Finland the costs of asthma medication are partly refunded by the Social Insurance Institution of Finland. In contrast, medication costs of chronic bronchitis are not refunded. The net effect is that some patients with chronic bronchitis tend to be diagnosed as asthma for economic reasons. Since all diagnosed asthmatics were excluded, this minor diagnostic transfer strengthens our results.

The relationship between a risk factor (for example, occupation) and the prevalence of a disease (for example, chronic bronchitis) may be confounded by selection bias. A higher proportion of those with the symptoms of a disease will have stopped their exposure compared with those without symptoms. It is understandable, therefore, that there is a difference in the results of the cross sectional and longitudinal studies in relation to occupation. In this case, it should also be mentioned that the proportion of farmers in Finland has fallen considerably over the past 60 years. Before the second world war about 60% of the population were farmers and now less than 10% follow this occupation.

Our results confirm the finding obtained previously from studies among Finnish farming

population³: atopy predisposes to the development of chronic bronchitis. Furthermore, farming increases the risk of chronic bronchitis. The latter was established particularly strongly in the follow up study. Similar findings have been reported in studies in Italian farmers⁹ and grain handlers in both Canada^{10,11} and the USA.¹² In our present study the effect of atopy on the occurrence of chronic bronchitis was not as strong as in the previous Finnish study.³ In contrast, the effect of smoking was stronger than before. The differences could be explained by the fact that only a minority of the subjects in the present study were farmers. As suggested before,³ the heavy exposure of farmers to biological dusts may favour the development of both symptoms of atopy and of chronic bronchitis in subjects with atopic predisposition.

In conclusion, our study shows that atopy predisposes the development of chronic bronchitis in the non-farming population too. The results thus give further support to the Dutch hypothesis on the aetiology of chronic bronchitis. In addition to atopy and smoking, a farm environment is also a predisposing factor.

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