

# Hay fever, asthma and number of older siblings — a twin study

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## Summary

**Background** It has been suggested that allergic sensitization is inversely related to the number of siblings in the family.

**Objectives** To study whether a similar relation can be observed for hay fever and asthma among Finnish adolescents in a population with relatively low prevalence of atopic diseases.

**Methods** A questionnaire mailed to a nationwide sample of 1849 families with 16-year-old twins assessing the cumulative incidence of doctor-diagnosed hay fever and asthma among the adolescents and the number of older siblings in the family by parental report.

**Results** The cumulative incidence of hay fever was significantly lower among the adolescents with three or more older siblings (3.9%, 95% CI = 1.2–6.5%) compared with adolescents with fewer older siblings (12.7%, 95% CI = 11.4–14.0%). There was no difference in the cumulative incidence of asthma among the adolescents according to the number of older siblings in the family.

**Conclusions** Large number of older siblings appears to be protective against the development of hay fever.

**Keywords:** adolescent, asthma, epidemiology, family, hay fever, sibling

*Clinical and Experimental Allergy*, Vol. 27, pp. 515–518. Submitted 26 June 1996; revised 18 November 1996; accepted 30 November 1996.

## Introduction

As the prevalence of allergic diseases has increased in industrialized countries during the past decades, the need to understand the environmental factors responsible for this change has become urgent [1]. Definite answers on the role of air pollution, passive smoking, allergen load, and diet are still missing. However, there is some evidence for a preventive effect of a large family size against allergies. In a large prospective questionnaire study among British children followed up to adulthood the number of older siblings was found to be inversely related to the occurrence of hay fever [2]. Similar inverse relation between number of siblings and skin-test reactivity was observed among German schoolchildren [3]. The working hypothesis based on these results is that allergic sensitization can be

prevented by infections acquired during early childhood [2]. But could infections in early childhood actually have a protective effect against asthma, too? In the present paper, we report the cumulative incidences of hay fever and asthma among 16-year-old adolescents in relation to the number of older siblings in the family.

## Materials and methods

The Finnish Twin Cohort Study is a project for the study of genetic and environmental determinants of chronic diseases and risk factors [4]. Twin pairs born between 1958 and 1986 have been identified from Finland's Central Population Registry. For twins born from 1974 onwards, the number of twins identified from the Central Population Registry is nearly identical with the number of twins born annually according to birth statistics compiled by the Central Statistical Office of Finland [4].

Data were collected by questionnaires [5]. After a pilot

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**Table 1** Hay fever and asthma in 16-year-old Finnish adolescents according to the number of older siblings. Cumulative incidence with 95% confidence intervals

| Number of older siblings               | Adolescents with hay fever (n/N) | Cumulative incidence of hay fever (95 % CI) | Adolescents with asthma (n/N) | Cumulative incidence of asthma (95% CI) |
|----------------------------------------|----------------------------------|---------------------------------------------|-------------------------------|-----------------------------------------|
| 0                                      | 141/1144                         | 12.3%*<br>(10.4–14.2)                       | 36/1106                       | 3.2%<br>(2.3–4.4)                       |
| 1                                      | 135/1032                         | 13.1%<br>(11.0–15.2)                        | 41/992                        | 4.1%<br>(2.9–5.4)                       |
| 2                                      | 49/384                           | 12.8%<br>(9.4–16.1)                         | 10/376                        | 2.7%<br>(1.0–4.3)                       |
| 3 or more                              | 8/206                            | 3.9%*<br>(1.2–6.5)                          | 6/206                         | 2.9%<br>(0.62–5.2)                      |
| Total                                  | 333/2766                         | 12.0%                                       | 93/2680                       | 3.5%                                    |
| Cochran's $\chi^2$ test for trend [24] | $\chi^2$                         | 4.76                                        |                               | 0.12                                    |
|                                        | P-value                          | 0.03                                        |                               | 0.73                                    |

\* Difference of cumulative incidence = 8.4%, 95% CI=5.19–11.7%

n Number of cases.

N Number of adolescents.

study, a questionnaire was mailed to twins born in 1975 through to 1977 within 2 months of their 16th birthday inquiring about health habits, symptoms, as well as personality and social relationships. The parents of the twins were mailed a questionnaire about the birth, development and growth of the twins during early childhood and adolescence until age 16 [5]. Questions on chronic conditions and diseases such as asthma and hay fever were included. A total of 1858 families were contacted and 1516 questionnaires on twins' childhood were returned.

The occurrence of hay fever in the adolescents was assessed by parental responses to a question on whether the first-born twin, the second-born twin, neither twin or both twins had been diagnosed with hay fever by a doctor.

From this, the presence or absence of hay fever in each twin was determined. A similar item was used to assess a history of asthma diagnosed by a doctor in the adolescents. Also the number of older children in the household was asked.

## Results

In the 1516 families who responded, data on hay fever could be obtained for 91% ( $n=2766$ ) and on asthma for 88% ( $n=2680$ ) of the adolescents.

The cumulative incidence of hay fever was 12.0% and that of asthma was 3.5% (Table 1). There was no difference in the cumulative incidence of hay fever among the adolescents with none, one or two older siblings (12.3–13.1%).

**Table 2** Concordance for hay fever in 16-year-old Finnish twinpairs according to the number of older siblings. Number of concordant pairs, discordant pairs and probandwise concordance rate

| Zygoty    | Monozygous twins       |                      |                                  | Dizygous twins         |                      |                                  |
|-----------|------------------------|----------------------|----------------------------------|------------------------|----------------------|----------------------------------|
|           | Concordant pairs (n) * | Discordant pairs (n) | Probandwise concordance rate (%) | Concordant pairs (n) * | Discordant pairs (n) | Probandwise concordance rate (%) |
| 0         | 13                     | 19                   | 58                               | 14                     | 60                   | 32                               |
| 1         | 17                     | 17                   | 67                               | 13                     | 52                   | 33                               |
| 2         | 2                      | 2                    | 67                               | 8                      | 26                   | 38                               |
| 3 or more | 0                      | 2                    | 0                                | 0                      | 4                    | 0                                |

\* In concordant pairs both twins have hay fever.

However, the cumulative incidence of hay fever among the adolescents with three or more older siblings was significantly lower (3.9%) compared with the other subgroups (Table 1). When only one twin of each pair was analysed, the difference between the groups of none and three or more siblings remained significant (8.4%, 95% confidence interval = 3.76–13.0%). Also the declining trend for occurrence of hay fever with greater number of older siblings was significant (Table 1). When data on asthma were analysed, no significant difference in cumulative incidence could be observed between any of the subgroups (Table 1). There was no significant difference in the occurrence of hay fever in the first-born twins (11.5%) compared with the second-born twins (12.6%). Neither did the birthorder of the twins affect the occurrence of asthma (in first-born twins 3.4%, in second-born twins 3.5%).

The concordance for hay fever was similar in twins with none, one or two older siblings. Among twins with three or more older siblings, the concordance rate was zero, but based on only six discordant pairs. To further examine the relationship of family size to occurrence of hay fever, the concordance for hay fever was computed separately for monozygous (MZ) and dizygous (DZ) pairs. Pairs in which zygosity could not be determined were excluded from this analysis (Table 2). The concordance was higher among MZ twins compared to DZ twins overall and by the number of older sibs indicating a genetic effect for liability to hay fever.

## Discussion

Our study confirms and extends the previous results on an inverse relation between atopic susceptibility among children or young adults and family size [2,3].

While the sample consisted of twinpairs, this did not seem to affect the results, even though the selective effect of twinship can not be excluded. The low concordance for hay fever in families with three or more sibs may reflect differing contributions of genetic and environmental factors in such families compared to families with fewer older sibs. However, the small numbers may simply reflect sampling variation, because even a single concordant pair in this subgroup would have yielded concordance rates similar to those observed for smaller families. Studies with more families of twins would be needed to elucidate this further.

Previous population-based twin studies among adults have reported similar occurrences of hay fever and asthma as in corresponding studies on singletons [6,7]. Also in the adolescent twins, the occurrence of hay fever and asthma correspond with the recent allergy surveys from Finland. Among 15–16-year-old schoolchildren the prevalence of allergic rhinitis was 14% and that of asthma 2.5% [8]. In a nationwide sample of teenagers the point prevalences of self-reported doctor-diagnosed allergic rhinitis and asthma

were 14.9% and 5.0%, respectively, [9]. The parent-reported prevalence of doctor-diagnosed asthma in schoolchildren from eastern Finland was 4.4% [10]. We know of no evidence indicating that the occurrence of hay fever or asthma is different in twins and singletons.

It may be the case that hay fever and asthma are less likely to be diagnosed in younger children of large sibships for various reasons, such as parents paying less attention to symptoms in their fourth or fifth child as compared with their first or second one. However, at the same time parents will have learnt to recognize better serious symptoms and bring them to the attention of their doctor. Access to health care in Finland is not limited by financial constraints and primary health care centers serve the entire population. Also, objective measurements of atopic sensitization (skin-test reactivity) have shown the same inverse relation we observed [3,11]. Other family structure-related factors such as number of younger siblings, father's social class, and maternal age or parity have played a less important role in the development of hay fever in the proband compared with the number of older siblings [12]. It has entitled the hypothesis that exposure to infections from older siblings in early childhood can prevent allergic sensitization. The hypothesis is supported by the findings that allergic diseases are less common in populations where the incidence of respiratory infections is high [13,14]. The hypothesis is also in agreement with our increasing knowledge on immune responses in allergy. In the development of atopic constitution, the balance between T-helper-1 (TH<sub>1</sub>) and TH<sub>2</sub> cell clones has shown to be important [15,16]. Recurrent infections in early life may preferentially select TH<sub>1</sub> and inhibit TH<sub>2</sub> cell clones which produce cytokines essential for IgE dependent allergies. Although the antigenic environment in early childhood is an important regulator in the development of acquired immunity, the role of factors such as timing of infections, dose and spectrum of infectious antigens is not well understood [17].

Large family size did not decrease the occurrence of asthma among adolescents. Similar results to ours have been reported among British children. At the age of 5 and 16, there was no significant relationship between wheezing illness and the number of older children in the household [18]. Among British 1958 birth cohort followed up to adulthood, birthorder did not increase the incidence of asthma or wheezing illness at any age [19]. Neither did the family size affect the prevalence of asthma or bronchitis among Australian schoolchildren [20], while opposite results have been reported from New Zealand. Among schoolchildren there was a significant trend for declining prevalence of wheezing related to number of older children [21].

Due to the rather small numbers of asthmatic adolescents in each subgroup our result concerning asthma need to be

interpreted with caution. Our result may though indicate that environmental factors, other than family size, are more influential in triggering mechanisms underlying asthma. One possible explanation is that genetic factors contributing to the development of asthma are, at least partly, different from those of allergic rhinitis, as suggested by twin and family studies [7,22,23].

It is concluded, that large sibships appear to be protective against atopic sensitisation manifesting as hay fever also in a population with low prevalence of atopic diseases.

### Acknowledgements

The authors wish to thank Mr Torsten Winter for the data processing.

The study was supported by grants from PHS/AA-8315, Academy of Finland, Allergiatutkimussäätiö, Clinical Research Institute of Helsinki University Central Hospital, Ida Montin Foundation, Association for the Pulmonary Disabled, Paulo Foundation, and Suomen Astra Oy.

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