

## Familial Risk of Allergic Rhinitis and Atopic Dermatitis among Chinese Families in Singapore

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### Abstract

**Introduction:** This study aims to determine the familial risk of atopic dermatitis (AD) and allergic rhinitis (AR) in Chinese children. **Materials and Methods:** A cross-sectional study was conducted in a housing estate in Singapore. Data was collected using an interviewer-administered questionnaire. Participants included 257 Chinese families. Prevalence rate ratios (PRRs) and 95% confidence interval (CI) were calculated. **Results:** For AD in all children, an increasing trend was found with PRRs of 1.9 (95% CI, 0.3 to 11.8) and 1.5 (95% CI, 0.4 to 5.5) for only father and only mother affected, respectively, to 2.3 (95% CI, 0.4 to 13.7) for both parents affected. In AR, a PRR of 2.7 (95% CI, 1.8 to 3.9) and 2.2 (95% CI, 1.5 to 3.2) for only father and only mother affected, respectively, and 4.5 (95% CI, 3.3 to 6.1) for both affected was found. The PRR (2.2; 95% CI, 1.4 to 3.7) of the first child developing AR when paternal or maternal history was positive was similar. This rose to 3.4 (95% CI, 2.2 to 5.1) when both parents also had AR. The PRR of the second child developing AR was 3.9 (95% CI, 1.7 to 8.9) when the first child alone was positive for AR and 7.0 (95% CI, 3.5 to 13.9) when both parents and the eldest child had AR. **Conclusion:** A positive family history increases the risk of developing AD and AR with increasing risk dependent on number of relatives affected. The second child's risk of AR is also associated with AR in the first child, suggesting mechanisms of incomplete penetrance.

Ann Acad Med Singapore 2004;33:71-4

**Key words:** Allergic rhinitis, Atopic dermatitis, Atopy, Familial study, Singapore

### Introduction

Family history has been shown to be a risk factor for the development of allergic rhinitis (AR) and atopic dermatitis (AD).<sup>1-4</sup> However, the increase in prevalence has also been attributed to the changes in lifestyle and urbanisation in developed countries.<sup>5,6</sup> A few studies have been undertaken to investigate the familial risk of these diseases in Asia,<sup>4,7</sup> of which no detailed study in Singapore is currently available.

The clinical manifestation of AR is known to follow either the perennial pattern or the seasonal pattern, when it is also known as hay fever. In Singapore, only the perennial form of AR is present, as compared to the temperate countries where seasonal AR is the dominant form.<sup>8</sup> As such, the disease proves to be a problem of constant morbidity throughout the year with

no seasonal intervals of relief for its sufferers in this part of the world.

Furthermore, AR and AD are common conditions in Singapore.<sup>4,9</sup> The prevalence and severity of these diseases are rising globally. This is reflected in studies carried out in many Western countries,<sup>10-12</sup> and in some Asian countries, including Singapore.<sup>9,13-15</sup> This rise has also increased the strain on the healthcare budget both in Singapore<sup>16</sup> and elsewhere.<sup>17,18</sup> This study aims to determine the risk of children developing AR and AD with a family history of birth diseases.

### Materials and Methods

A cross-sectional study was conducted in January 2002 and included 2851 households in Blocks 201 to 237 in Bishan

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This project was supported by the Department of Community, Occupational and Family Medicine, Faculty of Medicine, National University of Singapore.

North housing estate, Singapore. Of these, 1222 households were selected by simple random cluster sampling. The inclusion criteria were: both parents must be Chinese; age of eldest child in family  $\leq 21$  years of age; and all family members must live in the same home unit. Thus, only 535 families were considered eligible.

Data were obtained using a questionnaire and physical examination. Apart from questions pertaining to socio-demographic characteristics, the questionnaire included questions from 2 internationally used questionnaires.<sup>19,20</sup> The questions for AR were extracted from the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire,<sup>19</sup> and those for AD from the United Kingdom (UK) Working Party's Diagnostic Criteria for Atopic Dermatitis.<sup>20</sup> Three modifications were made to suit the local population. The first change to the ISAAC questionnaire was omitting the question asking the individual in which of the past 12 months was sneezing or a runny or blocked nose present in the absence of a cold or the flu. In the second change, the term 'hayfever' was replaced with 'allergic rhinitis' as the former is not used locally. The only modification to the UK Working Party's Diagnostic Criteria for Atopic Dermatitis was to replace the term 'hayfever' with 'allergic rhinitis'.

The environmental factors explored include number of cigarettes smoked, presence or absence of pets and carpets, frequency with which bedsheets were changed, practice of burning incense or joss sticks, and presence of air pollution in the environment. The questionnaire was also translated into Chinese and back-translated into English for accuracy and consistency. All interviewers underwent standardised training in language, interviewing and physical examination skills to reduce biases.

The physical examination involved the inspection for flexural dermatitis on 5 sites: behind the knees, in front of the elbows, around the ears or eyes, in front of the ankles and the sides or front of the neck.

Non-contactables were defined as the failure to administer the questionnaire after 3 attempts, including 2 weekday and 1 weekend visits. Answering by proxy was allowed if a child was still absent after 2 attempts. A primary caregiver was allowed to answer the questions on the child's behalf and recall any flexural dermatitis using standard protocol pictures.

Data analysis was carried out using SPSS Version 10.0 (Chicago, IL, USA) to generate descriptive information and prevalence rate ratio (PRR) with 95% confidence interval (CI). A *P* value of  $<0.05$  was considered statistically significant. STATA Version 7 was used to calculate the prevalence rate (95% CI) to adjust for clustering.

The confounding effect of age and ethnicity were controlled by restricting the study subjects to Chinese families and children  $<21$  years old. The rest were addressed by statistical analysis of the relationship of the confounder with the development of AR in children and parental history of AR.

## Results

Of the 535 families who were considered eligible, 268 (50.1%) responded. Two hundred and fifty-seven completed questionnaires were collected and the results analysed.

Of the children surveyed, 84% were  $\leq 15$  years old and 52.5% were male. Among the parents, 92% had secondary level education and above. Most families either had 1 child (21%), two children (54.9%) or three children (23.0%). The majority lived in 4-room flats and had a household income  $>S\$3000$ .

Table 1 shows the prevalence of AD and AR according to gender, adult, child and age of the latter. The prevalence of AR and AD was higher in males, and in children than in parents.

In the analysis of familial risk in AD in children, an increasing trend was found: PRR rose from 1.9 (95% CI, 0.3 to 11.8) and 1.5 (95% CI, 0.4 to 5.5) for only father and only mother affected, respectively, to 2.3 (95% CI, 0.4 to 13.7) for both parents affected. In AR, a similar trend was observed: PRR rose from 2.7 (95% CI, 1.8 to 3.9) and 2.2 (95% CI, 1.5 to 3.2) for only father and only mother affected, respectively, to 4.5 (95% CI, 3.3 to 6.1). Because of small numbers, further assessment of AD was not done. The confounding effects of gender of child, pets, carpets and exposure to passive smoking were statistically insignificant.

To eliminate the effect of clustering, further analysis was done only with the AR status of the eldest child (Table 2). There was still an increasing trend from 1 parent affected to both, although the strength of association fell for only father affected, remained similar for only mother affected and fell for both parents affected.

The PRR of the second child affected with AR after accounting for both parental history, as well as the eldest child's history of AR, is shown in Table 3. An increasing trend is found for both parents who are AR-positive or only the eldest sibling who is AR-positive to both parents and eldest sibling who are AR-positive.

A positive association was also found for children with AD or AR when there is a positive parental history of atopy. The

Table 1. Prevalence of AD and AR in the Families

Variable	No. of AD cases per 100 individuals (95% CI)	No. of AR cases per 100 individuals (95% CI)
Overall	6.1 (4.6-7.5)	23.8 (21.2-26.4)
Gender		
Male	6.8 (4.6-9.0)	24.8 (20.4-29.3)
Female	5.3 (3.3-7.3)	22.7 (18.5-27.0)
Parents	3.1 (1.4-4.8)	21.0 (17.1-24.9)
Children (y)		
1-12	9.0 (6.4-11.6)	26.5 (21.9-31.2)
13-21	9.6 (6.5-12.7)	26.5 (21.3-31.7)
	7.7 (3.5-11.9)	26.6 (19.0-34.2)

AD: atopic dermatitis; AR: allergic rhinitis; CI: confidence interval

risk for the eldest child was 3.6 (95% CI, 1.7 to 7.9) and 2.3 (95% CI, 1.6 to 3.3) for AD and AR, respectively, if either parent was atopic. The risk of AD in the eldest child against a parental history of AR was also increased (PRR: 3.0; 95% CI 1.5 to 6.1), whereas that of the presence of AR in the eldest child with a parental history of AD was 1.9 (95% CI, 1.2 to 3.2). These values show an increased risk of acquiring AR or AD when there is a positive parental history of other atopic diseases.

**Discussion**

A strength of the study is the homogeneous sample: Chinese. An attempt was also made to reduce interviewer bias by standardisation of questionnaire translation and training of interviewers.

The prevalence of AR and AD obtained was 23.8% and 6.1%, respectively. However, this figure is only representative of a population selected using a set of stringent criteria. Hence, the result cannot be extrapolated to the general population or

be compared with other prevalence studies. Our study has shown that males had a slightly higher prevalence of both AR and AD compared to females. This is consistent with other studies.<sup>3,9,11</sup> However, this did not reach statistical significance and was probably due to the small sample. Both AR and AD also had a lower prevalence in parents compared to children, suggesting a negative correlation with age.

Although often taken to be synonymous with genetic risk,<sup>1</sup> a shared environment may also explain aggregation of diseases in a family.<sup>2</sup> However, shared environmental factors have not been shown to significantly affect familial aggregation in studies which include mathematical models, although their effects cannot be entirely ignored.<sup>1,21</sup>

An increase in risk of children developing AD was found when either parent had a positive history. This association increased in strength when both parents have positive histories. The result is consistent with the conclusions of a large cross-sectional study in Germany<sup>1</sup> which shows that genetic contribution from each parent has an additive effect. Similarly, the results for AR showed the same trend. We corrected for clustering by only considering the eldest child in each family who were assumed to be independent of other children. The same trend remained, although there was a fall in the strength of association, indicating that clustering may spuriously elevate the familial risk of AR. When we compared paternal influence to maternal influence, the familial risk was similar in both. This finding is consistent with a case-control study in Germany.<sup>2</sup> However, in that study, there was a greater maternal influence.<sup>1</sup> Hence, at this stage, the relative influence between father and mother may be considered equivocal.

The risk of AR and AD was also increased in a child with a positive parental history of any atopic disease, that is, AR, AD or asthma. This does not prove that the familial risk of any specific atopic disease, such as AR, is increased with a general allergic state of the parents, since this positive risk may be due to parental history of the specific disease. However, when we analysed the PRR of AR with a positive parental history of AD and vice versa (that is, a parental history of a different atopic disease), a significant risk was obtained. This finding is consistent with that of a cross-sectional study in Germany<sup>1</sup> and supports the notion that AR and AD are associated with familial transmission. We were not able to correct for clustering in this analysis because the resultant sample size, considering only the eldest child was too small.

The risk of the second child developing AR when either parent or the eldest child, or both, had AR was found to increase. These results may be explained by a mechanism of incomplete genetic penetrance.<sup>1</sup> The German case-control study had determined that the correlation of AR between siblings is significantly higher than that between parent and child.<sup>2</sup> However, we did not obtain this result in our study as the relative risk when the eldest child alone is positive is only slightly higher than the risk when the parents are affected. When both parents and the eldest child were positive for AR, the relative risk almost doubled, suggesting a mechanism of

Table 2. Risk of Eldest Child Having AR in Relation to Family History

Family history	Total	No. of affected eldest child (%)	PRR (95% CI)
None	169	35 (20.7)	1
Father only	28	13 (46.4)	2.2 (1.4-3.7)
Mother only	40	18 (45.0)	2.2 (1.3-3.4)
Father or mother	68	31 (45.6)	2.2 (1.5-3.3)
Father and mother	20	14 (70.0)	3.4 (2.3-5.1)
Parental*	88	45 (51.1)	2.5 (1.7- 3.5)

AR: allergic rhinitis; PRR: prevalence rate ratio

\* At least 1 parent is affected (including the condition where both are affected).

Table 3. Risk of Second Child Having AR in Relation to Family History

Family AR history	Total	No. of AR+ Second child (%)	PRR (95% CI)
None	109	9 (8.3)	1
Parental*	33	10 (30.3)	3.7 (1.6- 8.3)
Eldest sibling <sup>†</sup>			
Parental <sup>‡</sup>	28	9 (32.1)	3.9 (1.7-8.9)
Eldest sibling <sup>§</sup>			
Parental or Eldest sibling <sup>‡</sup>	61	19 (31.1)	3.8 (1.8-7.8)
Parental* Eldest sibling <sup>§</sup>	33	19 (57.6)	6.9 (3.5- 13.9)

AR: allergic rhinitis; AR+: allergic rhinitis-positive;

PRR: prevalence rate ratio

\* At least 1 parent is affected (including the condition where both are affected).

<sup>†</sup> Eldest sibling is not affected.

<sup>‡</sup> Neither father nor mother is affected.

<sup>§</sup> Eldest sibling is affected.

<sup>‡</sup> The condition where 1 of the 3 members of father, mother or eldest sibling is positive for the disease.

“higher susceptibility” genes.

This study has shown associations between family history of AD and AR and the expression of the disease. Further comparisons of familial risk may be a useful indicator of genetic preponderance in subgroups with different characteristics, such as ethnicity. Shek et al<sup>22</sup> have linked atopy to chromosome 5q31-33 in the Chinese population in Singapore. Elucidation of susceptibility genes, including ethnic-specific loci, will give important clues in genetic transmission. Finally, although a familial study alone does not truly investigate a solely genetic mechanism, as family units share a common environment, a clearer picture of the pathogenesis of these atopic diseases may be obtained when familial and genetic linkage studies are reviewed with those that explore the role of the environment.

### Acknowledgements

We thank Drs J Cheah, KS Chia, SM Saw and Mr WT Tang for their support and assistance, as well as Community Health Project Group 6 (CC Lam, A Jain, SY Ho, EH Kua, WT Sia, SH Ibrahim, SJ Juan, WS Lee, SY Leong, WM Tai, DN Tan, WC Wee, KF Yip, HC Lee, CH Ng, N Jauhar, S Thangaraju, S Singh, O Wijeweera, CY Lim, SY Lim, WF Ng, S Subramaniam, CH Yip, CT Ong and KS Ong) for their participation in this study. This study was organised and supported by the Department of Community, Occupational and Family Medicine, Faculty of Medicine, National University of Singapore.

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