



Letter

Effect of genetic factors on the development of atopy and reactivity to specific allergens

A twin study

Atopy designates the propensity of individuals to mobilize IgE-mediated immediate hypersensitivity reactions. It is widely accepted that heredity plays an important role in the development of overall atopy. Several studies have concluded that the overall risk of becoming atopic and the variation in total serum IgE levels are mainly controlled by genetic factors.^{1–3} However, whether the tendency toward developing allergy to specific allergens is controlled by genetic factors remains to be firmly established.

This study aimed to investigate the relative influence of genetic and environmental factors on the variation in tendency to atopy by comparing concordance rates for (1) overall atopy, (2) number of positive allergens in a standard skin prick test (SPT), and (3) the exact same allergens in monozygotic (MZ) twins vs dizygotic (DZ) twins, where at least 1 individual within the twin pair had asthma. Comparison of concordances in MZ and DZ twins allows us to estimate the degree of heredity of atopic conditions directed toward a variety of allergens.¹

Danish adult twin pairs born between 1953 and 1982 who were registered in the Danish Twin Registry, who were living in the geographic regions surrounding the study site (Copenhagen), and with at least 1 twin having self-reported asthma were invited to participate in the study. In total, 575 individuals participated, comprising 256 twin pairs, 89 MZ pairs, 167 DZ pairs, and 63 single twins. The single twins were not included in the analysis. The Committee of Biomedical Research Ethics of The Capital Region of Denmark approved the study.

In this study, atopy was defined as a positive SPT result. SPTs were performed using standard dilutions of 10 common aero-allergens: birch, grass, mugwort, horse, dog, cat, house dust mite (*Dermatophagoides pteronyssinus* and *Dermatophagoides farina*), and molds (*Alternaria iridis* and *Cladosporium herbarium*). Hypersensitivity was defined as a reaction with a mean wheal diameter of minimum 3 mm. A positive test result was defined as hypersensitivity to at least 1 allergen.

Statistical analyses were performed calculating pairwise concordances, which denote the probability that a twin is affected or will develop illness given that his or her cotwin is affected. Because the study population was selected through a proband with asthma, the pairwise concordance rate was used to measure twin similarity: $C/(C+D)$, where C is the number of concordant twin pairs and D is the number of discordant twin pairs. Concordances were calculated for overall atopy (positive SPT result), same number of positive allergens, and for reactivity to exactly the same allergens for MZ twins and DZ twins, respectively. Furthermore, concordances for specific allergens were calculated. It was not possible to calculate

concordance rates for molds (*Alternaria* and *Cladosporium*) because of the small number of cases.

The mean age of the study population was 35.9 years (range, 21–51 years), and 58.9% were females. The prevalence of a positive SPT result in the study population ($n = 575$) was 55.1%. SPT data were available for 89 MZ twin pairs of which 42 twin pairs were concordant and 20 were discordant for a positive SPT result. Of the 167 DZ twin pairs tested, 59 were concordant and 59 were discordant for a positive SPT result. Concordance for MZ vs DZ twins for overall positive SPT results was 0.68 and 0.5, respectively ($P = .23$).

Among the 42 MZ twin pairs concordant for a positive SPT result, 14 twin pairs were concordant for the same number of positive allergens, and 5 pairs were concordant for the exact same allergens. Among the 59 DZ twin pairs concordant for a positive SPT result, 6 were concordant for the same number of positive allergens, and 1 pair was concordant for the exact same allergens.

We found higher concordances in MZ twins compared with DZ twins for both number of positive allergens and hypersensitivity to the exact same allergens (0.33 vs 0.10, $P = .02$, and 0.12 vs 0.02, $P = .09$, respectively). Concordances for specific allergens in a standard SPT among MZ and DZ twins are given in Table 1. The MZ twins had a higher concordance than the DZ twins for sensitivity to birch, grass, ragweed, horse, dog, cat, and *D farina*. The difference was significant for birch, ragweed, and dog, suggesting that the propensity to become allergic to these specific allergens is inherited.

Our findings indicate an influence of genetic factors on the development of sensitivity to specific allergens. Despite numerous studies in this field, results are still inconsistent. Several studies^{4–6} have confirmed a strong genetic influence on overall atopy but provided limited support for genetic control of hypersensitivity to specific allergens. Previous studies^{6,7} suggest that genetic control of hypersensitivity to specific allergens is less extensive than that controlling overall atopy. Other studies^{8,9} have, on the contrary, found that genetics are decisive in developing atopic reactions to house dust mite, cockroach, and peanuts. Altogether, the results thus far have been inconsistent, and there is still much left to be investigated in the field of heritability and atopy.

One criticism of twin studies is that they may overestimate heritability. This criticism is attributable to the tendency of parents to raise MZ twins more similar to one another and in general assent their similarities compared with DZ twins. Another critical concern is the tendency of MZ twins to choose similar environments in which to live. These circumstances would lead to a relative higher

Table 1Resemblance between Danish twins for overall positive SPT results, same number of positive allergens, same specific allergens, and each specific allergen^a

Zygosity group	No. of pairs	No. (%) of affected pairs	No. of discordant pairs	No. of concordant pairs	Concordance rate	P value
Positive SPT result						.23
MZ	89	63 (69.7)	20	42	0.68	
DZ	167	118 (70.6)	59	59	0.50	
Same No. of positive allergens						.02
MZ	89	42 (42.2)	28	14	0.33	
DZ	167	60 (35.9)	54	6	0.10	
Same specific allergens						.09
MZ	89	42 (47.2)	37	5	0.12	
DZ	167	59 (35.3)	58	1	0.02	
Specific allergens						
Birch						.01
MZ	88	28 (31.8)	14	14	0.50	
DZ	166	68 (40.9)	57	11	0.16	
Grass						.06
MZ	89	47 (52.8)	20	27	0.57	
DZ	166	78 (47.0)	54	24	0.31	
Ragweed						.02
MZ	89	14 (15.7)	7	7	0.50	
DZ	166	40 (24.0)	35	5	0.13	
Horse						.64
MZ	89	16 (17.9)	13	3	0.19	
DZ	166	23 (13.9)	21	2	0.09	
Dog						.04
MZ	89	44 (49.4)	30	14	0.32	
DZ	166	54 (32.5)	48	6	0.11	
Cat						.12
MZ	89	55 (61.8)	39	16	0.29	
DZ	166	62 (37.3)	53	9	0.15	
<i>Dermatophagoides pteronyssinus</i>						.81
MZ	89	50 (56.8)	36	14	0.28	
DZ	166	55 (33.1)	38	17	0.31	
<i>Dermatophagoides farinae</i>						.54
MZ	89	44 (49.4)	32	12	0.27	
DZ	166	40 (24.1)	32	8	0.20	
<i>Alternaria</i>						NA
MZ	89	0	0	0	NA	
DZ	166	9 (5.4)	8	1	0.11	
<i>Cladosporium</i>						NA
MZ	89	0	0	0	NA	
DZ	166	2 (1.2)	2	0	NA	

Abbreviations: DZ, dizygotic; MZ, monozygotic; NA, not applicable; SPT, skin prick test.

^aPairwise concordances are calculated by the formula C/C+D, where C is the number of concordant pairs and D is the number of discordant pairs. The pairs were only included in the analyses if SPT data were performed for both individuals. This is why there are only 88 MZ pairs in the analysis for birch (89 pairs for the other allergens). The same explanation goes for the first 3 analyses, including 167 DZ pairs but only 166 DZ pairs for the specific allergens.

MZ concordance compared with that seen among DZ twins, thus leading to overestimation of the role of genetics. It is generally accepted, however, that these circumstances have only a minor effect, if any at all, on the validity of twin studies.¹⁰ Furthermore, we cannot be sure that the conclusions drawn from this study are specifically linked to twins only or whether they apply to the general population. Furthermore, we cannot be sure that the findings presented here are entirely specific just for individuals with asthma. In conclusion, this study found that genetics has an effect on the tendency toward developing atopy in general and on the tendency to become hypersensitive toward particular allergens.

Linnea Skov, BSc*

Howraman Meteran, MD*,†

Vibeke Backer, MD, DMSc*,†

Simon Francis Thomsen, MD, PhD, DMSc*,‡,§

*Respiratory and Allergy Research Unit

Bispebjerg University Hospital

Copenhagen, Denmark

†Institute for Clinical Medicine

Faculty of Health and Medical Sciences

University of Copenhagen

Copenhagen, Denmark

‡Department of Dermatology

Bispebjerg University Hospital

Copenhagen, Denmark

§Department of Biomedical Sciences

Faculty of Health and Medical Sciences

University of Copenhagen

Copenhagen, Denmark

hmeteran@gmail.com

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