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Genetic and environmental contributions to hay fever among young adult twins

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Summary
Background: The susceptibility to develop hay fever is putatively the result both of genetic and environmental causes. We estimated the significance and magnitude of genetic and environmental contributions to hay fever among young adult twins.
Methods: From the birth cohorts 1953–82 of The Danish Twin Registry 11,750 twin pairs were identified through a nationwide questionnaire survey. Subjects were regarded hay fever cases when responding affirmatively to the question 'Do you have, or have you ever had hay fever?' Latent factor models of genetic and environmental effects were fitted to the observed data using maximum likelihood methods.
Results: The overall cumulative prevalence of hay fever was 12.6%. Identical twins were significantly more likely to be concordant for hay fever than were fraternal twins ($P<0.001$). Additive genetic effects accounted for 71% and non-shared environmental effects accounted for 29% of the individual susceptibility to hay fever. The same genes contributed to the susceptibility to hay fever both in males and in females. In families with asthma, the susceptibility to develop hay fever was, in addition to genes, to a great extent ascribable to family environment, whereas the aetiology of 'sporadic' hay fever was mainly genetic.

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Conclusions: The susceptibility to develop hay fever is attributable to major genetic influences. However, effects of family environment and upbringing are also of importance in families where asthma is present. These results indicate that different sub-forms of hay fever may have different aetiologies.

Introduction

Hay fever is a disease of the airways, which is characterised by sneezing, itching, rhinorrhea, and nasal congestion often following exposure to aeroallergens.[1] In a variable number of cases raised blood levels of IgE and atopic sensitisation to specific allergens accompany it.[2] Hay fever is associated with asthma and atopic dermatitis and this phenotypic overlap is known to be to a great extent genetic in origin.[3,4] Hay fever affects an extensive number of individuals with perhaps as much as one-third of the population being affected.[1] A childhood and adolescent preponderance in disease risk has been found and prevalence rates are substantial almost irrespective of the geographical area of interest.[5]

Surveys that examine the causes of individual susceptibility to hay fever and associated atopic traits have consistently revealed a major impact of genetic factors in the aetiology. The correlation in liability between relatives exceeds what is observed among random sets of individuals from the population and even more so when relatives of increasing genetic relatedness are compared. Numerous, and to some extent, contradictory studies of atopic disease have ascribed the pattern of genetic transmission both to recessive, dominant, co-dominant and polygenic inheritance.[6] Additionally, a range of environmental influences are undoubtedly involved in the causal pathways of the disease, most likely in conjunction with an adverse genetic constitution.[7]

Studies of twins can provide useful information on the aetiology of complex respiratory phenotypes, such as hay fever. The classical twin study examines to what extent genetic and environmental factors contribute to the development of a disease. The rationale behind the classical twin study is that identical twins not only share all their genes, but also their upbringing and early environment. On the other hand, fraternal twins share, besides their upbringing and early environment, only 50% of their genes. Hence, if identical twins resemble each other more for a disease compared with fraternal twins, genetic factors are assumed to contribute to development of that disease.[8] Within the framework of the classical twin study it is possible to partition the causes for individual susceptibility to develop a certain disease into the effects of genes, family environment, and individual specific environment.[8] Studies that have addressed these issues have shown that the heritability of hay fever, i.e. the proportion of phenotypic variance ascribable to genes, is ranging from approximately 35% to 80%. Furthermore, familial aggregation of hay fever has been found to be much less due to environmental influences shared between family members, while unique environmental influences obviously are important when explaining individual differences in disease occurrence.[3,4,9,10] Studies arriving at these conclusions have mainly been conducted within children and young adolescent populations, while nationwide samples of young adults only have been studied to a limited extent.

In order to estimate the relative impact of genetic and environmental influences on individual susceptibility to hay fever we undertook a comprehensive nationwide questionnaire survey among young adult Danish twins.

Methods

Study design

The study population is based on the twin cohorts born between 1953 and 1982 in Denmark who were enroled in the nationwide Danish Twin Registry.[11] In these cohorts zygosity was established in 1991 using four questions of similarity and mistaken identity, which have a frequency of misclassification of less than 4%.[12] In 1994, a total of 34,076 twin individuals, who in 1991 have declared their willingness to participate in future studies, were sent a questionnaire with items aimed at identifying multiple phenotypes including hay fever and asthma.[13] The participation rate was 86%, comprising 29,183 subjects (12,356 intact twin pairs and 4471 single responders). Among the 12,356 intact pairs, a total of 11,750 pairs with complete data on zygosity and hay fever were identified and analyses were based on this sample. Subjects were regarded hay fever cases when responding affirmatively to