Genetic Factors in Nickel Allergy

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Atopic disorders represent common and debilitating diseases, with a rising incidence over the last 30 y. Almost 30% of the population is affected by a form of atopic disorder. Many study designs have attempted to elucidate the role of genetic and environmental factors in the causation of atopy (Cookson and Moffat, 1999). This task is not simple, as the pathogenesis of atopy is complex, with the likelihood of gene–environment interactions. The relative contribution of genes and environment in the pathogenesis of atopy is not known, but numerous studies have shown that atopy clusters in families. It is likely that many different genes are responsible for an individual's predisposition to allergy and that exposure to certain known and unknown allergens leads to the expression of asthma, eczema, or hay fever. Twin studies have also been useful in estimating the relative importance of genes and environment on atopy, including eczema (Schultz Larsen, 1993; Lichtenstein and Svartengren, 1997; Strachan et al, 2000). Studies based on more than 3000 UK female twins have shown heritability estimates for eczema of 60%, with models being in favor of a combination of additive genes and unique environment (Mikkilineni et al, 2001). Candidate gene approaches for putative atopy genes have already been conducted by many groups in diverse populations, mainly using the family design (Ono, 2000). Many genes appear to have modest effects on the risk of atopy, and using genome-wide scans many chromosomal regions have been linked to the risk of atopy.

The study published in this issue by Brydl et al assesses the relative effects of genes and environment on the nickel allergy in a large population-based sample of female twins. Nickel allergy is a very common disorder affecting 30% of the population with a rising incidence, especially in females who have previously had skin piercing. The potential association between nickel allergy and atopy is controversial, as some studies have shown that nickel allergy is more prevalent in some atopic patients, whereas others have shown no association. Positive prick tests and IgE levels have not been shown to be associated with nickel allergy. Allergic contact dermatitis is dependent on cell-mediated immune response mediated mainly by type 1 lymphocytes, whereas atopic dermatitis is the result of sustained activation of type 2 lymphocytes, but little is known about the true relationship between nickel allergy and atopy. Another potential link between atopy and nickel allergy is the altered barrier function in patients who have atopic hand dermatitis, which may allow greater risk of contact allergy and therefore perpetuate the hand dermatitis. The twins in the study reported here were first recruited on the basis of having “hand eczema”. Clinical symptoms of hand dermatitis may be the manifestation of allergic contact dermatitis, irritant contact dermatitis, and atopic eczema—which may include dishyhidrotic eczema—thus the background phenotype of inclusion in this study may be very heterogeneous. The authors conclude that nickel allergy is unlikely to have a genetic basis because of the lack of a greater correlation in identical pairs compared with non-identical pairs.

Twin studies are ideally suited to dissecting genetic and environmental influence on a disease or trait, as opposed to family studies that are confused by common environmental influences that cannot clearly be separated from shared genes. But the estimates yielded by twin studies, however, are only applicable to the population studied and the method of ascertaining the twin pairs will also have a significant influence on the results. The study presented here by Brydl et al recruited highly selected twin pairs on the basis of one of the twins having had a history suggestive of “hand eczema”. Six hundred and thirty female twins who fulfilled the criteria for inclusion were selected from the Danish Twin Registry. On a background of “hand eczema”, the authors assessed the potential genetic influence on nickel allergy by patch testing. Although it is possible that nickel allergy is mostly influenced by environmental factors, the fact that the twins were recruited on the basis of a variable phenotype of hand eczema may have affected the results and interpretation. The sample size in each age group is also small and the power to discriminate genetic and environmental effects may also be an issue. This study has concluded that given a genetic susceptibility to atopy, there is no major additional genetic component to nickel allergy. Although it is evident that environmental factors such as ear piercing are important, as the prevalence of nickel allergy is much lower in men, the fact that only a proportion of the female population develops allergy to nickel suggests that genetic factors may also play a role. Studies have also shown some familial clustering in nickel allergy, supporting a genetic basis (Fleming et al, 1999). If the specific question about the true role of genes and environment in nickel allergy needs validation, the study should be repeated in an unselected random twin population of sufficient size.

DOI: 10.1111/j.0022-202X.2004.23508.x

References


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