Environmental factors and gene-environment interactions in the aetiology of asthma

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The importance of early life influences on aetiology of asthma in later life is implied by the observation of cohort factors underlying time trends in the disease and evidence that childhood characteristics predict persistence or new incidence of the disease in adult life. One potential mechanism for the long-term effect of events in childhood is the programming of memory T-cells to elaborate pro- or anti-inflammatory responses upon subsequent re-exposure to allergens. However, factors influencing the development of airway structure and function in early childhood may also have long-term consequences.

Earlier cross-sectional studies established a strong association between atopy (sensitisation to environmental allergens) and asthma. This led to a paradigm in which atopy was an intermediate stage in the development of asthma and further, exposure to those allergens was critical to the aetiology of both atopy and asthma. However, recent findings have cast doubt on this paradigm. The importance of other environmental and genetic factors, which may have a confounding or interacting effect, has been increasingly recognised.

Having a greater number of older siblings or attending childcare, having early life exposure to pets, and having lived on a farm as a child have all been consistently associated with a reduced risk of allergic illness. These observations have been linked to the “hygiene hypothesis”, for which a biological model based on influencing T cell differentiation has been proposed. However, in contrast to the consistent findings reported above, attempts to identify actual environmental exposures, such as endotoxin, *Mycobacteria*, or other infectious agents, which might mediate this effect, have yielded heterogeneous results. Genetic variation may explain some of the differences between studies.

At present there is no unifying theory to explain the childhood origins of asthma and hence no solid basis for developing preventive interventions. Progress towards this goal requires better understanding of the heterogeneous nature of the disease in early childhood, improved characterisation of relevant environmental exposures, and long-term follow-up of birth cohorts with reliable and valid measures of allergy and asthma outcomes.