

ENVIRONMENTAL INFLUENCES AND INFECTION AS AETIOLOGICAL AGENCIES IN ATOPY AND ASTHMA IN YOUNG CHILDREN		
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Summary

Atopy, and one of its common sequels, asthma, are increasing to an alarming extent particularly in developing countries. Genetic, environmental, infectious, dietary, occupational and sociological factors are all in various way implicated. This programme concentrated on children living in Europe to determine how a variety of quantifiable environmental factors, including nitrogen dioxide, tobacco smoke and dominant allergens interact with common childhood infections and dietary patterns in leading to atopy and asthma. The project was undertaken as a concerted action at seven sites in five Community States in urban and rural environments to take account of a variety of environmental and socio-economic factors. The aim was to derive more confident and intelligence based strategies of primary prevention.

Cohort Studies

Birth cohorts were established in; Ashford, UK; Barcelona, Spain; Menorca, Spain; Munich, Germany and Kuopio, Finland by recruiting pregnant women in their second trimester. In this way 2,500 children constituted the collective cohort. Aeroallergen and irritant exposures were measured in the home in the first two months of life, early respiratory symptoms were collected by annual questionnaire and in two of the centres an estimate of

bronchial responsiveness in children at 5½ years was made using peak flow responses to exercise tests. Breast feeding practices and the introduction of solids were also measured. Specific sensitisation was gauged by collecting venous blood samples at age 4 years which were then assayed for specific IgE to *Der p 1* (house dust mite) and *Fel d 1* (cat dander). Atopy at age 5½ was assessed in using skin prick test results to cat, house dust mite and grass pollen.

Cross-sectional Studies

In Crete children between 7-18 years attending schools in four different rural areas were invited to take part. Parents completed a questionnaire on respiratory and allergic symptoms, farming upbringing and confounding exposures. The children were skin prick tested to locally prevalent allergens.

In Poland, all families living in six villages south of Wroclaw and a nearby small town were invited to take part. Each family completed a questionnaire as above and were skin prick tested to local allergens.

Important programme findings, within the three year concerted action, are summarised as follows :

- **exposure-response relationship to domestic aeroallergens.**
There were no linear relationships between early allergen exposure and the induction of childhood respiratory allergy; rather the risks of IgE sensitisation and asthma rise at very low level of exposure and are attenuated thereafter. These patterns are influenced by parental atopy and birth order. The findings suggest important gene-environment interactions in the development of atopy and asthma and imply that reductions in domestic allergen exposure alone are unlikely to have a major impact in decreasing the incidence of these diseases in childhood.
- **respiratory irritants**
Nitrogen dioxide (NO₂) has been related to respiratory infections in experimental studies but its role remains controversial in general populations of children. We did not find any association of indoor NO₂ with any of the different indicators of lower respiratory tract infections in three birth cohorts of infants using individual passive samplers for measuring NO₂. The data suggest that the NO₂ effects on respiratory infections in outdoor air at current levels are probably due to other pollutants that have the same source and environmental dynamics.
- **early diet**
The results provided no evidence for a substantial protective effect of the late introduction of solids and subsequent development of toddler wheezing, transient wheezing, atopy or eczema. In fact, the late introduction of egg was associated with a statistically significant increased risk of eczema. There was no statistical evidence of feeding practices playing a role in the development of asthma and eczema after stratification for parental asthma and atopy status. These results do not support the recommendations given by present solid feeding guidelines stating that a delayed introduction of solids is protective against the development of asthma and allergy.
- **lack of 'farming effect' in Crete**
In an early study we reported that the prevalence of childhood atopy in a rural Cretan community was half of that in Iraklion, the capital city. Among rural children however there was no relationship between atopy and parental farming. To investigate this further we designed a second more detailed, cross-sectional survey to include children living in a variety of different rural setting on the island. Children with regular animal contact - at any stage in life - were equally likely to be atopic or to have current wheeze as children with less frequent or no contact. On the other hand children who currently lived in homes where sheep or goats were

kept nearby were less likely to be atopic, although they had an equal prevalence of current wheeze. The results indicate that while childhood atopy is not uncommon in this rural Cretan community, symptoms consistent with associated allergic disease are rarely reported. Despite clear differences in their contact with farm animals at all ages, we failed to find any consistent differences in the rates of atopy and allergic disease between those children whose parents are or are not farmers. It is likely that these contrasting results are due to differences in farming and its protective qualities across Europe.

- **Poland and protection of a rural childhood**

The findings are still under scrutiny but some interesting patterns are already apparent. While the rates of atopy among those living in the villages are the lowest ever recorded in Europe, those among the townspeople are similar to rates measured in the highest prevalence areas such as the United Kingdom. The expected age-related patterns is obvious in the townspeople with the highest prevalence among young adults; an attenuated pattern is apparent among the village population. From a cross-sectional design such as this it is not easy to separate age- from cohort-related effects but stratified analyses suggest that the patterns cannot be explained solely by a fall in allergy due to increasing age. The 'dose-response' observed for village life suggests a (protective) causative relationship. Consistent with this is the pattern of increasing urbanisation with age in this population. If this is the case then this comparison may serve as a paradigm for the emergence of allergic disease among (other) European populations. The nature of the protective factor(s) remains to be elucidated - and will be the focus of further study in this region.

Asthma and associated allergies affect children across Europe although there are wide geographical differences in prevalence that appear to be related to a 'western European' environment. The (residual) factors that determine these diseases may vary similarly. By examining populations with very different childhood environments this project has contributed to an increased understanding of these variations. Thus sibship and inheritance appear to be universally important while early exposure to domestic allergens and other pollutants is not. A rural upbringing is strongly protective at every age in Poland but is not in Crete, a difference probably attributable to dissimilar farming practices. Although these findings indicate that preventive strategies will need to be targeted appropriately, they suggest also that new approaches can be developed from the experience of different European communities.

Dissemination to appropriate audiences - including the study populations and the wider population of European families with young children - was an important part of this programme. An investigation into the most efficient and effective methods of dissemination was developed and implemented. Written materials, in particular brochures and newsletters, were the most welcome and seemingly most effective medium for communicating the aims and outputs of the study.