

## ABSTRACT

### Atopy in children - association to life style

Johan Alm

Sachsska barn- och ungdomskliniken, Institution Södersjukhuset,  
Enheten för klinisk allergiforskning, Institutionen för medicin vid Karolinska sjukhuset,  
Enheten för miljömedicinsk epidemiologi, Institutet för miljömedicin,  
Karolinska Institutet

The prevalence of allergic diseases has risen; in some countries nearly half the children suffer from some type of hypersensitivity. The reason for this increase is obscure, but one explanation is suggested to be a changing panorama of microbial stimulation early in life. The overall objective of this work was to study the effect of certain life style factors on the development of atopy in children.

In the first study the role of early BCG vaccination for development of atopy in children was investigated. A retrospective cohort study included 216 Swedish children with atopic heredity, born between 1989 and 1992, who received BCG vaccination when they were younger than 6 months. Comparison was made with 358 age-matched un-vaccinated controls. In the BCG vaccinated group 29% were atopic, defined as positive serology and/or skin-prick test, compared to 24% in the control group. Risk factors for atopic disease were evenly distributed between the two groups. It may be concluded that early BCG vaccination in children with atopic heredity does not play an important role for development of atopic disease before school age. To assess gene-environment interactions the distribution of promoter alleles on the NRAMP1-gene and for a nearby micro satellite, D2S1471, was investigated in blood cells from the children in the first study. Atopy in relation to NRAMP1 was similarly distributed between the two groups. In the BCG vaccinated children, however, genotype associations were observed for D2S1471 and atopy (Odds Ratio (OR) 4.3 [95% Confidence Interval (CI) 1.7-10.7]). Thus, stratification by BCG vaccination unmasked a genetic risk factor for atopy in the region of the NRAMP1 gene.

The anthroposophic life style has several characteristics, which are of interest in relation to atopy, such as restrictive use of antibiotics and vaccinations, and a diet containing live lactobacilli. In a cross-sectional study, 295 children at anthroposophic (Steiner) schools were compared with 380 children of the same age at neighbouring schools. At the Steiner schools, around half as many children had been treated with antibiotics and antipyretics, and had few vaccinations as compared to the control schools. Vegetables fermented by lactobacilli, were eaten by 2/3 of the children at Steiner schools, but rarely by the controls.

A lower prevalence of atopy, defined by objective tests, was shown in children from Steiner schools (OR 0.62 [95% CI 0.43-0.91]) including an inverse relation between the number of characteristic features of the anthroposophic life style and atopy ( $p=0.01$ ). Life style factors associated with anthroposophy appear to reduce the risk of atopy in childhood.

A role of intestinal microflora in turning the immune system towards tolerance is proposed. An anthroposophical way of life, including giving birth at home, may affect the intestinal microflora in infancy. In a cross-sectional study the intestinal microflora in 69 infants with an anthroposophical life style was compared with 59 children of the same age with traditional life style. Breastfeeding and use of antibiotics correlated to faecal microflora, and to fatty acids produced by indigenous bacteria. The effect of antibiotics on the flora seemed to be long lasting. The diversity of lactobacilli and presence of caproic acid were higher in infants born at home, than in those born in hospital. These differences may contribute to the lower prevalence of atopic disease previously observed in children in anthroposophic families.

Thus, new aspects on the importance of genotype-environment interactions in determining susceptibility for atopic disease have been highlighted. In addition, our results show that life style influenced atopy prevalence in school children and the composition of the gut flora in infants.

*Key words: anthroposophy, atopy, BCG, children, life style, microflora, NRAMP1*