

Atopy: A mirror of environmental changes?

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Allergen-specific IgE can be detected in cord blood,^{1,2} and prenatal exposures have been identified to determine atopic sensitization at school age.³ These findings fit well into a concept of early-life inception of atopic sensitization and disease. In a mouse model this hypothesis has been verified by protective prenatal effects on allergic asthma.⁴

In this issue of the *Journal*, Sozańska et al⁵ present a report, "Atopy and allergic respiratory disease in rural Poland before and after accession to the European Union," in which they demonstrate that the prevalence of atopic sensitization increased dramatically within 9 years in a rural area of Poland. The most striking finding is that the increase in the prevalence of atopic sensitization affected all age groups. This challenges the notion of the early origin of atopic sensitization.

The authors had the unique opportunity to collect questionnaire data on atopic diseases and assess skin prick test (SPT) response positivity in the same population 9 years apart. One might argue that the time lag might be associated with changes in measurement instruments, resulting in a spurious increase in SPT response positivity. However, this increase was much more pronounced in the rural than in the urban population. The specificity of this effect renders a systematic bias extremely unlikely. Moreover, the discrepancy between rural and urban populations is informative in itself. The authors suggest a farm-related exposure or better its loss as the driving force in the increase of atopy in the rural population. Rural and urban environments differ in a multitude of interrelated exposures; hence associations with distinct farm-related exposures on an individual level are impossible in this data set. Moreover, observational studies do not achieve the same level of evidence as experiments, although one might consider the described phenomenon an "experiment by nature."

The stratification for the town versus village populations reveals 2 distinct phenomena. To focus on these, we have created [Fig 1](#) from the original figures on the study population

participating in both surveys. We have grouped the findings by year of birth instead of age. The differences between 2003 and 2012 hence reflect the age difference between the surveys. In the town population only a marginal increase was seen. With increasing age, there was a tendency toward decreasing prevalence, except for a dip in subjects born between 1973 and 1982. This might be related to a weaker response rate in highly mobile educated young people with a higher propensity of atopy.

In contrast, in the village population the increase in atopy prevalence was much more pronounced and affected all age groups, which is suggestive of a cohort effect. As proposed by the authors, this effect might be attributable to the agricultural changes in the context of Poland's accession to the European Union in 2004.

The second phenomenon reflected by [Fig 1](#) relates to a much stronger and statistically significant increase in the villagers born between 1943-1952 and 1993-1997. Contrary to town children, there was a much more pronounced development of atopy during adolescence among the villagers. Children younger than 6 years were not included in the study population; hence effects on sensitization in early life could not be assessed. Even so, this phenomenon might be attributable to additional determinants in adolescents on top of the age effect. Interestingly, the birth years of this particularly susceptible age group (1993-97) point toward fundamental political and economic changes in Poland, when trade liberalization was introduced abruptly in the early 1990s.⁶ These changes involve higher mobility, societal diversity, smaller family size, novel foods, altered eating habits, transformations in the health care system, and others.

A parallel to this steep increase in atopy with fast economic changes can be seen in Poland's western neighbor: the German reunification in 1990 similarly revolutionized the East German economy, and atopy prevalence caught up with West German figures within a decade.^{7,8} In contrast to Poland, an even faster increase was seen in *cities* with more than half a million inhabitants, such as Leipzig, where the prevalence doubled within 3 years.⁸ This observation adds another aspect to the Polish study because it might point to profound societal and economic changes beyond agricultural transformations. Also in Poland an atopy-protective lifestyle might have been abandoned first in urban and subsequently in rural regions. In any case the parallel developments in Poland, Germany, and the Baltic countries, such as Estonia,⁹ underpin the robustness of environmental effects on atopy in childhood and beyond.

Hay fever prevalences increased also in both the Polish and German studies, whereas in Poland asthma prevalences remained stable thus far. This might be explained by a longer latency for the loss of specific rural exposures to affect asthma.

Taken together, these new data from Poland are exciting because they demonstrate the high plasticity of the allergic immune response also in adolescence and adulthood. Similarly, in adults protective environments can affect atopy, as has been

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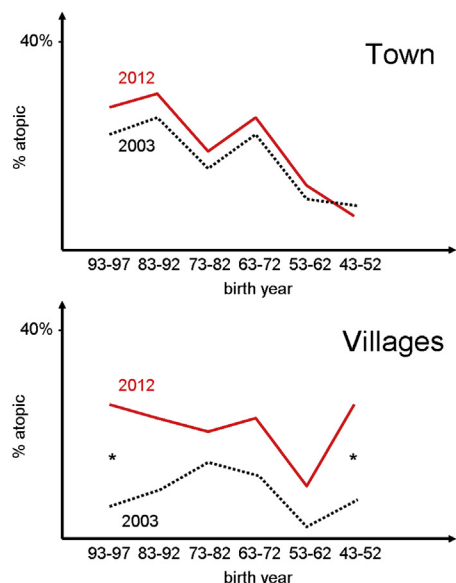


FIG 1. Increase in atopy prevalence over time by year of birth. This figure is a modification of Figs 2, B and D, from the article by Sozańska et al.⁵ For illustrative purposes, the prevalences in 2003 and 2012 are given for birth years instead of age groups. Asterisks mark significant differences, as determined by nonoverlapping CIs in the original figure.

shown in Danish farmers who did not spend their childhoods on farms.¹⁰ These had a 5 times lower chance of producing specific IgE to any allergen compared with never farmers.

The question remains whether the demonstrated plasticity also includes reversibility of atopy. Data from Austrian farm children indeed suggest cessation of atopy; they had an 8 times higher chance to lose SPT response positivity compared with children

not living on farms.¹¹ If this effect were also seen with other environmental exposures relevant for atopy and applied to manifestation of atopic disease, a whole new area of secondary prevention would emerge.

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