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Original article

Atopy and asthma in rural Poland: a paradigm for the emergence of childhood respiratory allergies in Europe

Background: We hypothesized that, in south-west Poland, a 'rural' protective effect on atopy and respiratory allergies would be most pronounced among children but that at all ages would be stronger among those with a rural background.
Methods: A cross-sectional survey of the inhabitants (age >5 years, $n = 1657$) of Sobotka, a town of 4000 people in south-west Poland: and seven neighbouring villages. We measured and analysed responses to skin prick tests (atopy) and to a standard questionnaire (asthma and hayfever).
Results: Atopy was very uncommon (7%) among villagers at all ages but not among townspeople (20%, $P < 0.001$); the differences were most marked among those aged under 40 years. Asthma and hayfever were similarly distributed, both being very rare among villagers. The differences appear to be explained by the cohort effect of a communal move away from rural life. This interpretation is supported by an ecological correlation ($\rho = -0.59$) between rural populations and childhood wheeze in 22 European countries.
Conclusion: The very striking differences in the prevalence of allergy between these two neighbouring communities of central Europe reflect the pan-continental population movements that may have been responsible for the emergence of childhood allergies in Europe.

B. Sozanska[1], S. J. MacNeill[2], M. Kajderowicz-Kowalik[1], H. Danielewicz[1], M. Wheatley[2], A. J. Newman Taylor[2], A. Boznanski[1], P. Cullinan[2]

[1]Department of Paediatrics, Allergology and Cardiology, Wroclaw Medical University, Wroclaw, Poland; [2]Department of Occupational and Environmental Medicine, Imperial College (NHLI) and Royal Brompton Hospital, London, UK

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Dr Paul Cullinan
Department of Occupational and Environmental Medicine
Imperial College (NHLI)
1b Manresa Road
London SW3 6LR
UK

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One of the more intriguing features of the epidemiology of respiratory allergies is their distribution across Europe. Asthma and allergic rhinitis are common among children living in the north-west of the continent but far rarer in more eastern and southern populations (1). The differences are about fourfold and unlikely to be explicable by genetic variation alone. Comparisons of genetically similar populations living under different circumstances provide further support for one or more important environmental determinants (2). International contrasts may hide even greater local differences. In some communities, children who have been brought up on farms have far fewer atopic diseases than do their nonfarming neighbours. This is attributed to one or more protective exposures that accompany a farm upbringing.

The high prevalence of these diseases in countries such as the United Kingdom and those of Scandinavia is believed to have arisen recently (3) although it has been difficult to identify exactly when. The increase is often – if loosely – attributed to 'westernization' although, again, the relevant details of this process remain largely mysterious. Most epidemiological research in this subject is of children. In part this is because the incidence of allergic asthma and rhinitis is highest in childhood and important environmental determinants must operate at that age; schoolchildren are also easily assembled in large numbers. Far less is known about the distributions of these conditions at older ages.

We report a cross-sectional survey of atopic disease in two neighbouring populations of people aged between 5 and 92 years living in Poland. We hypothesized that a 'rural' effect would be most pronounced among the children of these communities; but that at all ages those with a rural background would be less likely to have atopic disease.

Methods

Sobotka is a small market town in Lower Silesia, south-west Poland. Its 4000 inhabitants are involved chiefly with service industries locally or in Wroclaw, the provincial capital 50 km to the north. The town's population has not changed importantly in size over the past century; concurrent with the political changes in Poland in the 1990s several small-scale industries closed about 10 years ago.

Using a map provided by the town council we selected at random two distinct areas of Sobotka for survey. Similarly and again at random we selected seven villages from those situated 10 km or less from the eastern edge of the town. The populations of the surveyed

villages ranged from 47 to 288. As above the size of these villages has not changed for many years although in the 1990s farmers gained greater access to chemical fertilizers, pesticides and herbicides and the numbers of livestock diminished.

In 2003, with the assistance of community leaders we invited all households in the seven villages and in the two areas of Sobotka to take part in a survey of allergic disease. All who were aged 5 years or more and were considered residents of the households were eligible. Each person aged more than 15 years completed a questionnaire administered by a research nurse; mothers supplied information for children under the age of 16. We included standardized questions from the ISAAC protocol (4) to enquire into symptoms and diagnoses of allergic and other respiratory diseases; and into places of residence and (parental) occupations throughout life. We invited everyone to undergo skin prick testing with extracts of four common aeroallergens: house dust mite, cat fur, mixed grass pollens and tree pollens (ALK-Abelló, Hungerford, Berkshire, UK) and with negative (saline) and positive (histamine) control solutions.

To administer the questionnaires and perform skin testing we employed and trained six local nurses. Working in pairs they each surveyed equal numbers of urban and rural households; none was informed of the nature of our hypotheses until fieldwork was completed.

We received approval for the study from Ethics Committees at the University of Wroclaw and at Imperial College (NHLI) in London. Each participant provided signed consent and/or did so on behalf of their child.

Analysis

We defined a household as 'farming' if that was the principal source of its income. We considered allergen skin prick tests to be 'positive' if they induced a wheal of mean diameter 3 mm or greater than the response to saline. Persons are described as atopic if they had one or more positive allergen skin tests.

For continuous variables, we assessed differences between communities using the Wilcoxon rank sum test; and for categorical variables the chi-squared test or Fisher's exact test as appropriate. The chi-squared test for trend was used to assess trends in the prevalence of atopy across lifetime exposure to farming. Logistic regression models, stratified by age group, were used to examine the independent effects of village living. The models were clustered by family and adjusted for age, sex, first born status, maternal age and current smoking. Parental farming and animal ownership (at age 1) were added to the model individually to assess their impact on the variable 'village residence'. The results of these regression models are presented as adjusted odds ratios with 95% confidence intervals. All analyses were performed using SAS (SAS Institute Inc., Cary, NC, USA) and STATA (Stata Corporation, College Station, TX, USA) software.

For the ecological analyses and to examine urbanization we collected information on total and rural populations of European countries in 1950, 1980 and 2000 from the Food and Agricultural Organisation of the United Nations (5). For some countries – Estonia, Latvia, Slovakia and the Czech Republic – population figures for 1980 had to be derived by linear interpolation of data provided only for 1950 and 2000. For most of these countries we were able to estimate the mean prevalence of current asthmatic symptoms among children aged 13–14 years from the International Study of Allergy and Asthma in Children (1); for four countries – Bulgaria, Hungary, Slovakia and the Czech Republic – we obtained prevalences from a separate study (6) of slightly younger (7–11 years) children. The correlation between asthma symptoms and the proportion of a country's population that was classified as rural was determined using Spearman's rank correlation coefficient. Maps of Europe were generated in ARCVIEW GIS 3.2 (ESRI, Redlands, CA, USA).

Findings

Participation

Of 1928 eligible participants, 1700 (88%) completed a questionnaire and 1657 (86%) completed an interpretable series of skin prick tests. Those who took part were on average a little younger than those who did not (median age 36 years *vs* 39 years), were more often female (54% *vs* 38%) and resident in Sobotka (42% *vs* 34%).

The oldest participant was aged 92 years. Those living in Sobotka were on average a little older (40 years) than those from the villages (34 years, $P = 0.011$) but there were no differences in the sex distributions of the two communities. Family sizes in Sobotka were a little smaller (median four members, compared with five in the villages, $P < 0.001$) and consequently participants there were more likely to be first born (58% *vs* 49%, $P < 0.001$). Townspeople of working age were most commonly occupied in clerical work (12%), sales work (10%) or unspecified manual occupations (8%). Thirty-five percent of villagers aged between 20 and 65 years were farmers; 7% were employed in sales work.

Almost two-thirds (61%) of those now living in Sobotka had always lived in a town; this proportion was closely related to age such that 94% of those aged between 5 and 20 years but only 20% of those aged over 60 had always lived in a town. The remainder had migrated to Sobotka from villages. Almost all those (91%) living in a village had always done so, a proportion that did not vary by age. Very few (1%) of those living in Sobotka, but 55% of those in the villages, reported that they currently lived on a farm.

Prevalence of atopy and atopic disease

Ninety-six percent of people in each community had a positive skin prick response to histamine. The mean histamine wheal diameter was a little lower in the town population (4.63 mm) than in the villagers (4.99 mm); there was no important variation by age.

Specific skin tests were most often positive to extracts of grass pollen or house dust mite. Twenty percent of those living in Sobotka were atopic, a figure significantly higher ($P < 0.001$) than for those living in any of the villages (7%). This difference was present at all ages (Fig. 1) but most pronounced for those born between 1983 and 1992 (ages 11–20) where 35% of townspeople but only 8% of villagers were atopic. Among the people of Sobotka there was a marked variation in the prevalence of atopy by age, it being most common in those who were born after 1963 and far less common among the elderly. This pattern was attenuated among the villagers in whom there was very little variation in prevalence by age. In Sobotka, young men were more likely than young women to be atopic but there were no other important sex differences.

The frequencies, within the last 12 months, of wheeze and of seasonal rhinitis, both with evidence of specific sensitization (to any allergen and to a pollen, respectively), were distributed similarly and are displayed in Fig. 2. Each, but in particular atopic wheeze, was less prevalent than atopy. The distributions by age were very similar to those of atopy and again each was more common among townspeople.

The odds ratios for the association between atopy and current village habitation are depicted in Table 1. The 'village' variable remained statistically significant after adjustment for age, sex, smoking, first born status and maternal age and was shifted only

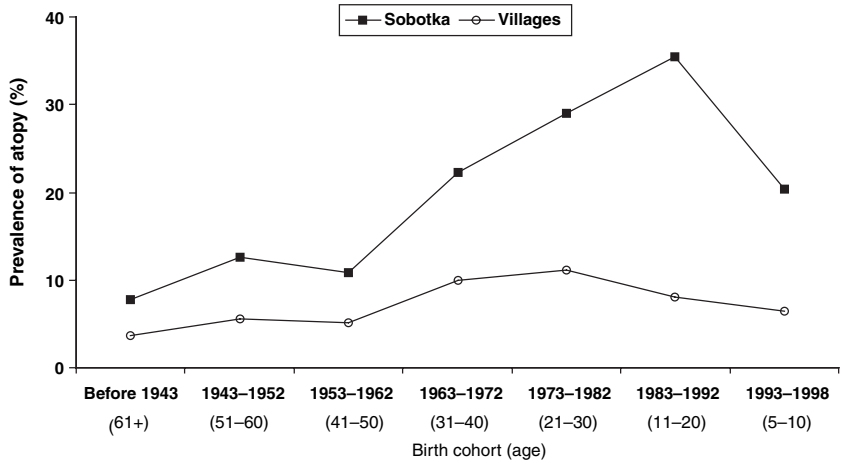

Figure 1. Prevalence of atopy by birth cohort and place of current residence.

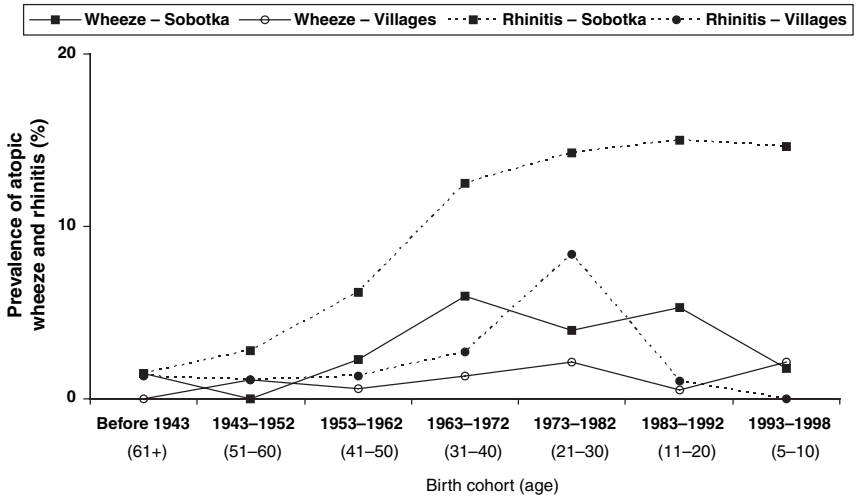

Figure 2. Prevalence of atopic wheeze and rhinitis by birth cohort and place of current residence.

Table 1. Adjusted odds ratios and 95% confidence intervals, derived by logistic regression, for the association between atopy and current village habitation

		Model		
	N	Core	Farming	Animal
All				
5–20 years	467	0.22 (0.12–0.40)	0.33 (0.16–0.67)	0.33 (0.17–0.67)
21–40 years	489	0.36 (0.22–0.60)	0.58 (0.32–1.05)	0.56 (0.31–1.03)
41–60 years	524	0.43 (0.22–0.84)	0.49 (0.24–1.02)	0.43 (0.22–0.88)
61+ years	220	0.44 (0.13–1.49)	0.38 (0.12–1.23)	0.41 (0.13–1.33)

Core model: includes age, sex, first born status, maternal age, current smoking and village residence.
Farming model: includes age, sex, first born status, maternal age, current smoking, village residence and parental farming.
Animal model: includes age, sex, first born status, maternal age, current smoking, village residence and family farm animal ownership (age 1).

marginally towards the null by further adjustment for a farming childhood or family ownership of farm animals during infancy. Further adjustment for consumption of unpasteurized milk during childhood made no difference to these estimates. The patterns were essentially identical in four age categories although the effect of current village living diminished by age.

Using information collected by questionnaire we constructed three categories summarizing the proportion of a lifetime spent in a village (Table 2). In all but the oldest of four age categories the prevalence of atopy was highest among those who had never lived in a village, lowest in those who had always done so – and intermediate in those who had moved between the two. We did not have sufficient information to examine the effects of age at migration from village to town or vice versa.

Ecological analysis

Figure 3 depicts the ecological association between symptoms of current asthma reported among European children in the mid-1990s and the proportion of their country's population that was classified as 'rural' in 1980, the approximate year of their birth. The correlation was strongly negative ($\rho = -0.59$); only two countries (the UK and Ireland) had rates of asthma clearly higher than those predicted by the line of least squares. In this analysis the prevalence of asthma symptoms in Poland was 8%; the corresponding figure in

Table 2. Proportion of study population by place of lifetime residence and birth cohort (age)

	All		1983–1998 (5–20 years)		1963–1982 (21–40 years)		1943–1962 (41–60 years)		<1943 (61+ years)	
Cohort (age)	*N* (%)	Atopic, *n* (%)	*N* (%)	Atopic, *n* (%)	*N* (%)	Atopic, *n* (%)	*N* (%)	Atopic, *n* (%)	*N* (%)	Atopic, *n* (%)
Never lived in a village	431 (25.4)	105 (24.9)	158 (33.8)	49 (31.4)	136 (27.8)	41 (31.1)	123 (23.5)	15 (12.4)	14 (6.4)	0
Moved between town and village	367 (21.6)	46 (12.8)	35 (7.5)	5 (14.3)	95 (19.4)	17 (18.7)	170 (32.4)	19 (11.2)	67 (30.5)	5 (7.9)
Always lived in a village	902 (53.1)	58 (6.6)	274 (58.7)	19 (7.1)	258 (52.8)	23 (9.0)	231 (44.1)	11 (4.8)	139 (63.2)	5 (3.9)
P-value (trend)		<0.001		<0.001		<0.001		0.009		0.683

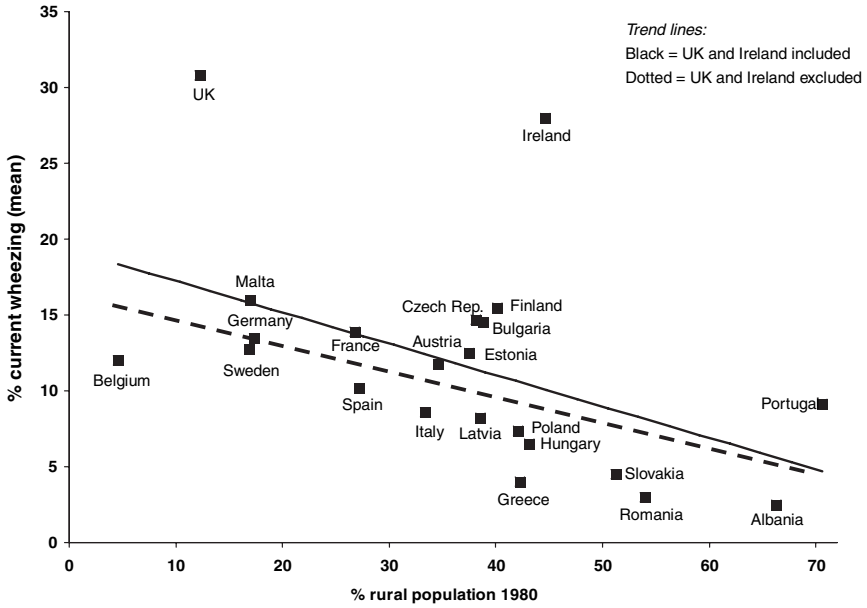

Figure 3. Ecological association between national rates of childhood wheeze and rural population in 22 European countries.

our survey was 3%. Using the same technique we observed a very similar pattern for seasonal rhinitis in the same populations (data available on request). In Figure 4 is depicted the marked shift from rural to urban living in Europe between 1950 and 2000; and in Figure 5 the steep decline in farming among the parents of those from our study who are now aged 20–40 years.

Discussion

There are remarkable differences in the prevalences of atopy and associated allergic diseases between two central European communities living in very close proximity. Our estimate of the prevalence of atopy in these villagers in south-east Poland is among the lowest ever recorded; in stark contrast, atopy among the residents of a small, nearby town appears – especially among young people – to be almost as common as it is in the highest prevalence areas of western Europe. Allergic asthma and rhinitis are each uncommon but again especially so in villagers. The differences are most apparent among the cohort born after 1960 and especially those who have always lived in a town. It is this generation too that has experienced the greatest shift from farming, a pattern reflected across Europe since 1950.

Much of the literature reporting urban–rural differences in allergic diseases relates only to children and some refers to non-European communities with high rates of parasitic infection and high prevalences of positive skin test responses (7–11); these findings are not easily compared with ours. Studies of European populations have had inconsistent results. In a survey of a population aged 25–75 years in southern Germany (12) farmers (22%) and 'villagers' (29%) were less often atopic than those who lived in small towns (33%) or a city (34%). These rural prevalences are notably higher, and the urban–rural difference smaller, than those we recorded. This probably reflects a difference in definitions – in the German survey a 'village' was defined as a settlement with < 5000 inhabitants – but it may also be that rural life in Germany is in some important respects different from that in contemporary Poland. A large survey of young adults in five European countries found a reduced prevalence of specific sensitization to cat fur and Timothy grass (but not house dust mite) in those who reported that they had lived on a farm during childhood (13). Positive relationships between community size and the prevalence of atopy have been reported from Italy (14), Germany (15) and the United States

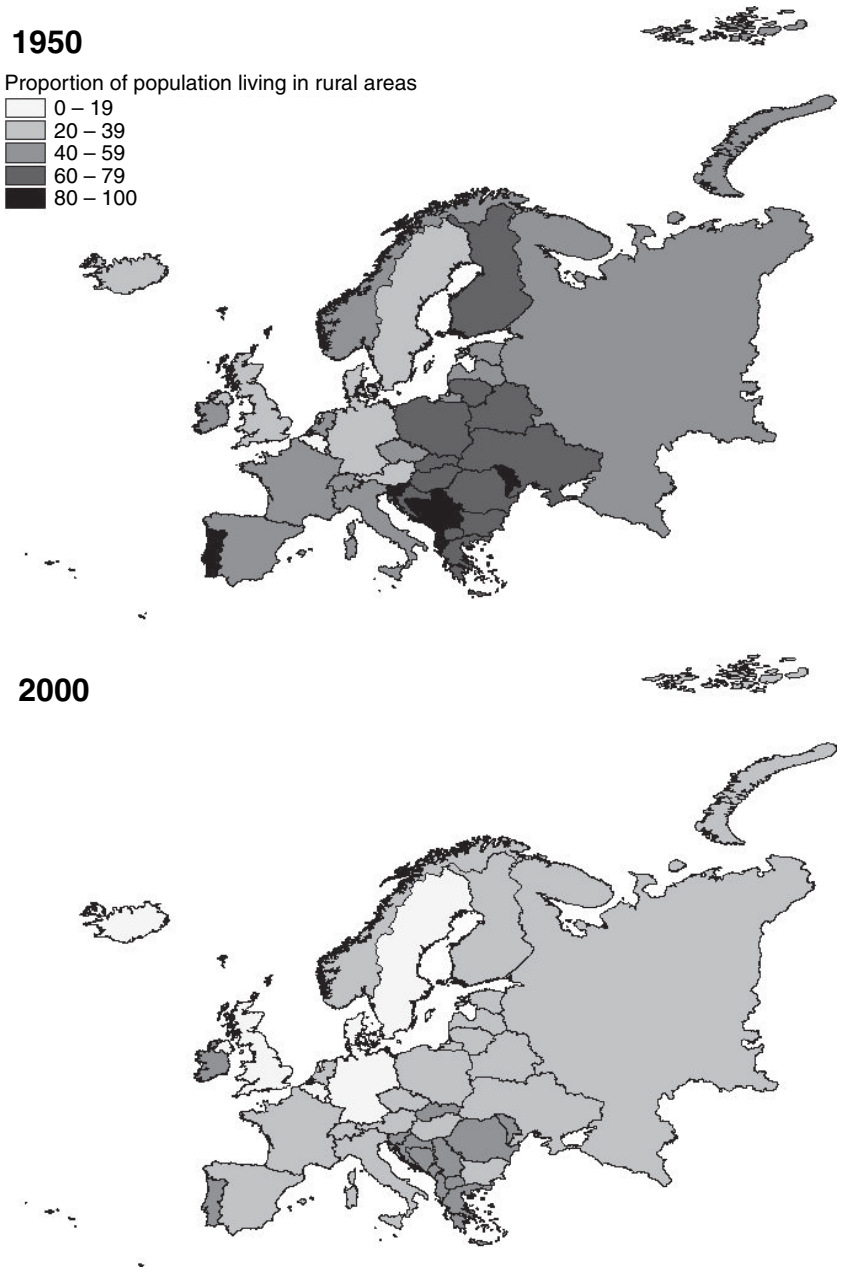

Figure 4. Urbanization in Europe 1950–2000.

(16) although again the comparisons were made between communities of very different sizes and proximities to ours. In contrast, no important differences in allergy between urban and rural populations have been found in Norway (17), the Basque region (18), Italy (19) or the United Kingdom (20).

Interesting comparisons can be made between our findings and those of populations brought up in the former East and West Germanys. Both children and young adults from the East were less likely to be atopic than those brought up in the West (2, 15), a difference that cannot readily be explained genetically. In both communities the prevalences of atopy were higher than in our study – and far higher than in our village populations. Intriguingly the East–West differences were markedly attenuated among those aged 50 years or more (15) suggesting – as with our data – an important cohort effect; and among children rapidly diminished as unification proceeded (21). Studies of farm children in Alpine regions have indicated that they have lower risks of atopy and allergic disease than do their nonfarming village neighbours (22–24); again, with only one exception (23),

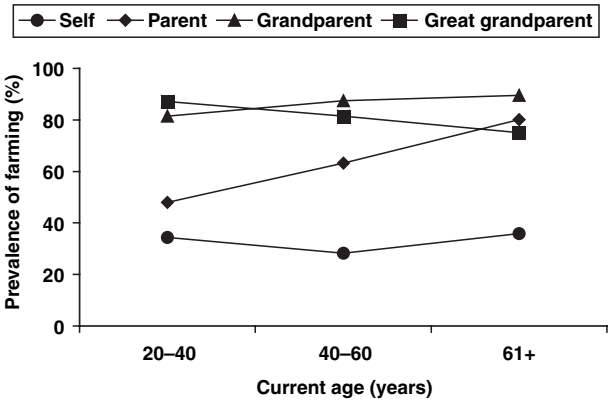

Figure 5. Prevalence of farming as main occupation by generation.

the prevalences even in farm children have been higher than those we measured. We could not entirely explain the differences between the Sobotka and village populations by a 'farming effect'. We surmise that this reflects the higher frequency of farming in these villagers (55%) than in Alpine communities (<4%). In effect, every villager here appears to be sufficiently exposed to the protective effect(s) attributed elsewhere to farming.

Our study is unusual for its inclusion of people at every age over 5 years. In Sobotka, the prevalence of atopy fell with advancing age, a pattern closely resembling that in the United States or western Europe (17, 25). In contrast, among the villagers in our study any age-related effect was barely perceptible. Thus, the distinction between townspeople and villagers diminished with age. The lower prevalence of atopy among the older residents of Sobotka probably reflects their higher frequency of sometime rural living, a 'cohort' effect. It may also reflect a decline in atopy with increasing age although there is scant evidence for such an effect. Longitudinal studies of both skin prick responses (26) and serum-specific immunoglobulin E (27) have not demonstrated any marked diminution in positive responses with advancing age. In contrast, a predominantly age-determined effect has been suggested by comparison of two cross-sectional surveys in the United States (25). The maximum span covered by these studies was 20 years (27) and any firm conclusions would have to await comparisons over longer intervals.

Objective measures of atopy are more specific and are more easily interpreted than subjective reports of allergic disease. Despite our finding that the patterns of allergic wheeze and rhinitis reflected those of atopy we have some misgivings about the validity of symptom reporting. We used in analysis responses to a questionnaire that was designed for the detection of asthma and hayfever in childhood; at older ages, particularly for diseases characterized by wheezing there is likely to be an important loss of specificity. Furthermore, it is not clear how meaningful is a translation, however accurate, of a questionnaire designed originally in English. Intriguingly the only countries where the frequencies of childhood wheeze differed markedly from the trend of our ecological analysis were those where English is spoken as a first language. Nonetheless – as they would apply equally to townspeople and villagers – we do not think that either of these issues had any important impact on our findings.

Charles Blackley, a physician working in Victorian England, noted – in 1873 – a remarkable absence of 'summer catarrh' (hayfever) among farmers, a phenomenon he attributed to what we would now call high-dose tolerance to pollen (28). Similarly he reported that hayfever was more common among city dwellers and suggested that the 'recent' (sic) emergence of the disease was a result of mass urbanization in 18th and 19th century England – and the collective loss of 'the preservative influence which a rural or semi-rural life exercises'. Unfortunately he provided no figures to support his observations but if they were accurate then they shed an interesting light on the 'hygiene hypothesis' – and perhaps also on the pre-eminence of English-speaking populations in the world of respiratory allergies. England was the first of the European nations to experience mass urbanization. In the 19th century childhood infectious diseases there were rife and mortality data indicate that they were far more common among children who lived in towns or cities than those in villages (29). The greatest differences were for deaths attributed to gastrointestinal and respiratory infections which were, respectively, about eight and two times more common among urban children. This would suggest that high rates of early life infections were not, in the context of Victorian urban England, necessarily protective against subsequent allergies.

We propose that the prevalences of atopy and allergy in the villages of lower Siliesia, at all ages, represent the 'native European state'; and those in Sobotka the effects of a progressive and communal move away from the land. If we are right then the findings reported here are a fortuitous snapshot of a pan-European communal process that was already apparent in Victorian England and that 20 years ago was in progress in the separated parts of Germany; a process whose remnants are still visible in Alpine villagers and in a continent-wide, ecological correlation between childhood allergy and urbanization. Its mechanisms remain unclear but, we believe, probably reflect the loss of a fairly specific, farm-related protective environment. It appears to be a process whose effects are rapid and likely to be accelerated by impending changes in European agricultural practices. If these proposals are correct then this region of south-western Poland is a socio-biological as well as a political 'microcosm' (30); and deserves further micro-geographical attention.

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