

Editorial

Allergic disease in urban and rural populations: increasing prevalence with increasing urbanization

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While recent studies from the developed western countries suggest that the prevalence of asthma and allergic disease may be reaching a plateau (1, 2), countries with communities in transition have experienced a dramatic increase over the last few years (3). The puzzle of the cause of this reported increase is complex, and there is no simple explanation or unique hypothesis that would be applicable for every phenotype or every population. Different environmental exposures including diet, hygiene and infections, allergens and air pollution, in combination with genetic factors could account for the observed variability.

In this issue of journal, Viinanen et al. present the data from a population-based study investigating the prevalence of clinically defined allergic diseases in urban and rural Mongolia (4). The results indicate a lower prevalence of allergies in rural Mongolia with increasing in prevalence with increasing urbanization. The authors suggest that differences in exposure to an agricultural environment (fermented milk products, herd animals) could possibly explain the observed differences. The findings are in line with what we have learnt from the majority of studies looking into differences between urban and rural populations worldwide.

Allergy in urban and rural settings

Differences in the prevalence of allergic disease between urban and rural areas have been observed in many parts

of the world. Such studies offered an excellent framework to investigate the potential risk or protective factors. Early studies from Africa (South Africa, Ethiopia, Kenya and Ghana) pointed out that populations living in rural areas (i.e. not exposed to the effects of an urban or western lifestyle) experienced a very low burden of allergic disease (5–8). A traditional rural way of living and the role of parasite infections were examined as possible protective factors. A series of studies from Asia (China, Japan, Korea, India and Saudi Arabia) confirmed the urban-rural gradient, exploring the role of exposure to different allergens, air pollution, affluence and diet in the development of allergy (9–13).

Rural farming vs rural nonfarming, 'old cities' vs 'new cities'

However, not every rural environment confers the same degree of protection. In Europe, attention has focussed towards studies exploring the differences between rural farming and rural nonfarming communities, since the risk of asthma and allergies was found to lowest amongst rural farming community (14–17). A 'protective' farming effect associated with a close contact to livestock, use of unpasteurized milk and increasing endotoxin exposure is currently under exploration, and the proposed gene by environment interactions involving important innate immunity genes offer insights into potential mechanisms (18).

Similarly, not every urban environment increases the risk of allergic disease. In South Asia a higher prevalence of wheeze (28.7 vs 12.5%) was found in children living in an old fashioned, congested, city than in a clean modern city with concrete housing, vehicle emission regulations and the use of smoke-free household fuel (19).

Definition of urban and rural areas

However, it has to be emphasized that studies from different parts of the world may not be comparable, as there are often important differences in the way urban and rural setting has been defined. In a nationwide study in Sweden according to the Population and Housing Censuses 'urban' is defined as a home located in a settlement with at least 200 inhabitants (15). In a recent study from the US, the nonurban population was defined on the basis of metropolitan statistical area codes (MSA) (US Department of the census) (20). MSA codes are numbered one to eight, with one denoting a district within a central city with a population of greater than 250 000. The following MSA codes were used to define the eligible 'rural' population: MSA (6) 'small town' = a small town not within an MSA and with a population of less than 25 000 and greater or equal 2500 people, MSA (7) 'rural outside an MSA' = a place with less than 2500 people and coded rural outside an MSA, and MSA (8) 'Rural inside an MSA' = a place with less than 2500 people and coded rural inside an MSA, by the census bureau. In the study from Mongolia subjects were randomly selected from an urban city, three rural towns and seven villages with a population of greater than 750 000, between 15 000–20 000 and 1000–2000 inhabitants, respectively. In a study from Kenya comparing EIB in urban and rural children, the subjects representing the urban population were selected from Nairobi, a city of over 2 million inhabitants (6).

It is obvious that a variety of different urban and rural definitions based on population numbers are used worldwide, making it difficult to compare studies from different continents. Furthermore, different populations may have different lifestyles and cultures, different environmental exposures and different genetic backgrounds.

Effect of urban living on different phenotypes

It is often implied that allergic sensitization, hayfever and asthma have increased in parallel. This, however, may not necessarily be true, and the increase in asthma may not be contemporaneous with, nor secondary to an increase in inflammation and allergic response with which it is closely associated (21). Studies of urban-rural differences appear to indirectly suggest that this is the case. Whilst a higher prevalence of allergy has consistently been reported in different urban areas, the observed pattern in terms of the effect on various allergy phenotypes (e.g. asthma vs sensitization) and identified risk factors has differed

between different studies. In the Mongolian study the prevalence of allergic sensitization and allergic rhinoconjunctivitis increased significantly with increasing urbanization, whilst asthma differed significantly from rural areas only in terms of severity, but not the prevalence (4). The pattern of sensitization was also different between urban and rural Mongolia, with sensitization to pollens being remarkably higher in urban areas. In Gambia, despite a relatively high prevalence of positive skin tests to aeroallergens in both urban and rural areas the prevalence of wheeze was not significantly associated with atopy (22).

The major difference between urban and rural areas may not be in the prevalence of these different phenotypes, but in the nature of their relationship: while atopy and wheeze appear to exist in rural settings unrelated to each other, the characteristic of most urban areas is a strong association between atopy and asthma.

Is 'affluence' responsible for the urban-rural differences?

The observed urban-rural differences may be confounded by the socio-economic status. In a study from Cape Town, Mercer et al. examined the relationship between symptom prevalence and severity, socio-economic status, recent urbanization and upward socio-economic mobility (23). The findings suggested an increased prevalence of rhinitis symptoms in the higher socio-economic group. Similarly, in Zimbabwe and Ghana the prevalence of exercise induced bronchospasm and atopy was found to be higher in urban rich than in urban poor children, indicating the importance of affluence rather than locality (Fig. 1) (8). However, in studies from Kenya, wealth status had no impact on asthma prevalence (6), and amongst rural children there was no association between immune responses to allergens and airway symptoms (24). In the US, an increased risk was reported for all children living in an urban setting regardless of race or income, suggesting that other environmental factors are important for the increased risk in urban areas (25).

Hygiene hypothesis within the urban-rural context

The Hygiene hypothesis states that environmental changes in industrialized world have led to reduced microbial exposure in early life, which resulted in the increased prevalence of allergic sensitization and disease (26). The association between reduced exposure to infectious agent and higher prevalence of allergy seems now to be confirmed by consistent evidence. Improved hygiene has generally been associated with increasing urbanization. However, in many US inner cities increased hygiene is most certainly not the problem, and despite relatively poorer hygienic standards in comparison to the rest of the population, there appears to be a marked increase in asthma among residents in the inner-city poor neighbourhoods (27).



Figure 1. Due to cultural and linguistic differences in the developing countries, it is often difficult to adopt a universally accepted definition of asthma and accurately compare the findings between different areas. To circumvent this problem, exercise induced bronchospasm is often used as an objective indicator of asthma (photos courtesy of Dr Emmanuel OD Addo-Yobo, Department of Child Health, Komfo Anokye Teaching Hospital, Kumasi, Ghana).

Furthermore, in a number of studies the increased risk for asthma in urban areas is independent of ethnicity or poverty (25). In South Africa, Steinman et al. reported that poor hygienic factors (including early exposure to farm animals) did not protect the rural Xhosa children from a dramatic increase in the prevalence of asthma and atopy over the past 20 years (28). These studies suggest that hygiene and genetic factors are not the only determinants of the increasing prevalence of asthma and atopy.

Air pollution and allergens and rising trends in respiratory allergies

High levels of vehicle emissions have been correlated with the increasing prevalence of respiratory allergies (29). Similarly, use of modern fuels appears to increase the risk of allergic sensitization and symptoms, and could be a significant contributing factor in the increasing prevalence of allergic disorders (30). Although the role of air pollution on the development of allergic disease is unclear, there is an increasing body of evidence suggesting that the higher levels of traffic related particles in combination with their ability to change the antigenicity of pollen may contribute to the increased prevalence and severity of allergic disease in urban areas (31).

Another recently proposed hypothesis suggests that the rising trends of allergy in urban areas may in part be explained by a decreased exposure to allergens such as pollens (caused by changes in urban lifestyle, e.g. more time spent indoors and away from areas abundant in natural allergen sources) leading to lower tolerance to pollens: 'a reverse case of immunotherapy' (32).

Conclusions

Differences in allergic disease between urban and rural areas exist and are real, but patterns vary across various phenotypes, and different causes may be responsible for the observed differences. Nevertheless, all of these studies emphasize the importance of environmental factors in the development of allergic diseases. Allergens, farming, animals and endotoxin, pets and parasites, air pollution, hygiene, infections and immunizations, breast-feeding, unpasteurized milk and diet, affluence, house construction and bedding, domestic fuel and smoking, family history and genetic variation are all pieces of the allergy puzzle. Urban-rural variability offers extreme ends of various environmental exposures, and allows a unique insight into the potential causes of increase in allergies. However, aware of the difficulties in the interpretation of data in urban-rural studies researchers in this field are becoming more specific in terms of definition of various potentially important environmental exposures, considering the poor/rich, farming/nonfarming and many other variables in an attempt to better understand the causes of the observed differences. The elucidation of mechanisms by which these environmental exposures affect not only the prevalence of sensitization and allergic disease, but also the relationship between different phenotypes (e.g. sensitization and wheeze) may help us understand the causes of the increase in allergic disease and facilitate the design of future primary prevention strategies.

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