

What can urban/rural differences in food allergy prevalence tell us about the drivers of food allergy?



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It is generally agreed that food allergy has become more common in developed countries around the world over the past 10 to 20 years. This increase in food allergy follows the previous increase in asthma and allergic rhinitis that first started more than 50 years ago. Although drivers for increasing rates of food allergy remain unclear, some aspect of the modern lifestyle is believed to be central to the increase.

Data from developing and underdeveloped regions of the world remain scarce as the health care systems in these regions continue to deal with issues related to infectious disease, trauma, and factors associated with poor sanitation and has not yet pivoted to focus on conditions associated with the 21st century, such as allergy, obesity, and cardiovascular disease. Interestingly, the World Health Organization is beginning to recognize and understand that even in one country, a “2-speed” economy can have differential effects on health outcomes, and therefore public health messages for the developed world need to consider factors that are associated with both urbanization and rural settings.

Increasing urbanization can have a direct negative effect on the prevalence of allergic disease. The “old friends” hypothesis proposes that a balanced immune system requires exposure to a diverse range of environmental and commensal microbes that were present during the evolution of the human immune system.¹ Exposure to these microbes is thought to activate immunoregulatory mechanisms that reduce the risk of the inappropriate immune reactions that characterize allergic disease. Furthermore, in parts of the world with heavy loads of these microbes, there has been selection for compensatory genetic variants that have a proinflammatory effect, which might lead to excessive inflammation if these microbial exposures are withdrawn. Living in urban environments is likely to reduce opportunities for contact with these microbes, such as reduced contact with farm animals, more time spent indoors, and less exposure to the natural environment.

The report by Botha et al² in this issue of the *Journal* is the first to describe food allergy prevalence in South Africa using data from the South African Food Allergy Study (Fig 1). The report, which also describes differences in food allergy prevalence between rural and urban areas in South Africa, is timely for several reasons. Data on food allergy prevalence from low- and middle-income countries are currently rare. Furthermore, this is the first study to describe differences in challenge-confirmed food allergy prevalence between urban and rural children within a single country. Understanding factors driving lower rates of food allergy in rural compared with urban areas might provide a key to unlocking the modern food allergy epidemic as we try to discover what aspect of an urbanized or modern lifestyle might be harmful.

Botha et al² report a prevalence of food allergy in urban South African toddlers in Cape Town of 2.3% (95% CI, 1.5% to 3.7%), which was significantly higher than the prevalence in the rural Mqanduli district of the Eastern Cape (0.5%; 95% CI, 0.1% to 1.8%). Of the 7 allergens tested (egg white, peanut, cow's milk, cod fish, soya, wheat, and hazelnut), the most common food allergy in both urban and rural areas was egg allergy (urban: 1.8% [95% CI, 1.1% to 2.7%]; rural: 0.5% [95% CI, 0.1% to 1.8%]), which reflects findings from other regions of the world (Table I).²⁻⁶ Similarly, peanut was the next most common source of food allergy in the urban cohort (0.7%; 95% CI, 0.3% to 3.1%). By contrast, and rather surprisingly, there were no other food allergies found in the rural cohort of 398 children, possibly because of the very low prevalence of food allergy in the rural area.

The study also explored potential differences in food sensitization and allergy prevalence in different ethnic groups (black African, mixed ancestry, and white) in the urban cohort. It should be noted that the rural cohort was entirely black African, and therefore the effect of ethnicity could not be explored in this context. Although there was some evidence of a difference in food sensitization between ethnic groups in the urban cohort, there was little evidence of a difference in food allergy prevalence, although the sample size for this comparison was limited, particularly in the white group (reflecting the ethnic demographics of children in this age group in Cape Town in general). As expected, food allergy was significantly more common in urban black African children compared with rural black African children.

As for all population-based studies, there are some limitations necessarily related to the limited resources available when conducting large studies, some of which are magnified in studies conducted in rural areas. The strengths of this study include the use of objective measures of food allergy outcomes consisting of skin prick testing to 7 foods conducted for all participants and food challenges for all sensitized subjects. Participation rates in the study were high for the study overall (>95%) and for oral food challenges (79%), and the authors also calculated adjusted food allergy prevalence estimates, taking into account missing data on food challenge outcomes for children who completed all the required challenges. Limitations include the use of a different

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TABLE I. Prevalence of challenge-proved IgE-mediated food allergy in infants and young children around the world

Country (reference)	Location	Setting (eg, urban or rural)	Study characteristics		Prevalence (% [95% CI])		
			Age	No.	Overall food allergy	Egg allergy	Peanut allergy
South Africa ²	Cape Town	Urban	12-36 mo	1185	2.3 (1.5-3.7)	1.8 (1.1-2.7)	0.7 (0.3-3.1)
	Mqanduli district	Rural	12-36 mo	398	0.5 (0.1-1.8)	0.5 (0.1-1.8)	0 (ND)
China ³	Chongqing	Urban	0-12 mo	497	3.8 (2.5-5.9)	2.5 (1.3-4.4)	0 (ND)
Australia ⁴	Melbourne	Urban	12 mo	5276	11.0 (10.1-11.9)	9.5 (8.7-10.3)	3.1 (2.7-3.6)
United Kingdom ^{5,6*†}	Southampton	Urban	0-2 y	872	2.6 (1.5-3.6)	2.1 (1.1-3.0)	0.6 (0.1-1.1)
Germany ^{5*}	Berlin	Urban	0-2 y	1440	—	2.0 (1.0-3.5)	—
Greece ^{5*}	Athens	Urban	0-2 y	844	—	0.1 (0.0-0.4)	—
Iceland ^{5*}	Reykjavik	Urban	0-2 y	1292	—	1.3 (0.8-2.0)	—
Italy ^{5*}	Milan	Urban	0-2 y	1007	—	1.6 (0.7-2.2)	—
Lithuania ^{5*}	Vilnius	Urban	0-2 y	1296	—	0.9 (0.1-3.3)	—
The Netherlands ^{5*}	Amsterdam	Urban	0-2 y	933	—	1.6 (0.8-2.6)	—
Poland ^{5*}	Lodz	Urban	0-2 y	1343	—	1.0 (0.4-1.9)	—
Spain ^{5*}	Madrid	Urban	0-2 y	1155	—	1.3 (0.6-2.4)	—

ND, Not determined.

*Egg allergy data are from the EuroPrevall birth cohorts.⁵ Estimates from EuroPrevall refer to the adjusted 2-year incidence of egg allergy and can also include cases of non-IgE-mediated egg allergy.

†Estimates for egg, peanut, and overall food allergy prevalence in the United Kingdom are taken from a separate publication from the United Kingdom cohort of the EuroPrevall project⁶ and include only IgE-mediated food allergy cases.



FIG 1. Rural (A and B) and urban (C) participants in the South African Food Allergy Study. Images were supplied by Dr Michael Levin.

recruitment method for the urban cohort (recruitment at early childcare centers) compared with the rural cohort (raising awareness through local primary health care clinics and community stakeholders) necessitated by the fact that there are few early child care centers in the Mqanduli district. In addition, although the authors undertook an *a priori* sample size calculation for the main research question of interest, some subanalyses, particularly those related to ethnicity-based differences in food allergy, were limited by small subsample sizes.

These are among the first population-based food allergy prevalence data using challenge-confirmed food allergy outcomes

from an African country⁷ and therefore are incredibly important if we are to understand more fully the global burden of food allergy. Because South Africa is one of the more urbanized environments within Africa, we might expect a lower food allergy prevalence in other African countries, but it would be valuable for other African countries to obtain baseline data on the allergy epidemic, even if only through indirect measures, such as questionnaires.

Outside of Africa, food allergy prevalence has been investigated in rapidly developing China. In a study of infants in Chongqing in 2009, 3.8% (95% CI, 2.5% to 5.9%) had a challenge-proved food allergy, most commonly to egg, followed

by cow's milk.⁸ There is emerging evidence that the prevalence of food allergy might be increasing in China with increasing urbanization, with a separate comparison of 2 cross-sectional studies 10 years apart in Chongqing reporting an increase in food allergy between 1999 and 2009 among infants aged 0 to 24 months.³

Evidence from our work on migration and food allergy provides some potential insights into the effect of urbanization on food allergy prevalence. We showed that challenge-confirmed food allergy was 3 times more common in infants with parents born in East Asia compared with those with parents born in Australia.⁹ This increased risk appears to have occurred in a single generation because the prevalence of reported allergic disease was similar or even lower in Asian-born parents themselves compared with Australian-born parents. Furthermore, we showed in a separate study that children born in East Asia who subsequently migrated to Australia in early life were protected against food allergy.¹⁰ This supports a gene-environment interaction in food allergy risk whereby those genetically at risk are protected from expression of allergy if born in the country of their parents, whereas those born into a country of migration are at increased risk. Migration is likely to be associated with changes in a number of factors, including humidity (with an effect on skin dryness and skin barrier), latitude (and therefore vitamin D exposure), diet, and microbial exposure (the "old friends" hypothesis). These factors could act through a number of mechanisms to increase the risk of food allergy. Genetic polymorphisms more prevalent in the Asian population because of selective pressures of the Asian environment might increase the risk of allergy when these environmental factors are removed after migration. Although exposure to some of these factors (eg, humidity) might change little with increasing urbanization, microbial exposure in particular is likely to undergo significant changes.

Finally, this current article, along with emerging evidence from other developing countries, suggests we can anticipate increasing rates of food allergy as part of the lifestyle evolution occurring in

these countries. This provides a window of opportunity for bodies of public health experts, such as the World Health Organization and World Allergy Organization, to step in and using the existing evidence base ensure that public health guidelines are optimally used to protect the developing world from the underbelly of the 21st century improvements in health. Only time will tell whether the developing world can learn from the lessons of the developed world to get ahead of the negative health effects of the modern lifestyle.

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