

Original papers

QJM

Domestic risk factors for wheeze in urban and rural Ethiopian children

D. DAGOYE¹, Z. BEKELE¹, K. WOLDEMICHAEL¹, H. NIDA¹, M. YIMAM¹, A.J. VENN², A. HALL³, J.R. BRITTON², S.A. LEWIS⁴, T. MCKEEVER² and R. HUBBARD²

From the ¹Faculty of Medical Sciences, Jimma University, Jimma, Ethiopia, ²Division of Epidemiology and Public Health, University of Nottingham, Nottingham, ³London School of Hygiene and Tropical Medicine, University of London, London, and ⁴Division of Respiratory Medicine, University of Nottingham, Nottingham, UK

Received 20 January 2004 and in revised form 14 April 2004

Summary

Background: To identify which environmental exposures underpin the emergence of asthma epidemics, we need to study epidemics as they appear, as is now happening in the Jimma region of Ethiopia. We have previously studied risk factors for asthma in adults in Jimma and have now completed a survey of young children.

Aim: To establish the prevalence of asthma in urban and rural children in Jimma, and to identify locally important risk factors.

Design: Cross-sectional survey.

Methods: All children aged 1–5 years living in Jimma town and three surrounding rural regions were identified. Data were collected using an interviewer-led questionnaire, and consenting children had skin prick tests to house dust mite and cockroach.

Results: We surveyed 7155 children, of whom 3623 (51%) were female and 4285 (60%) lived in the urban area. The prevalence of wheeze in the last year was 3.4%, and was lower in the rural area (OR 0.47; 95%CI 0.34–0.66). In the urban area, the main risk factors for wheeze were a longer duration of breastfeeding, use of kerosene, and environmental tobacco smoke, while living with animals was protective. In rural children, the main risk factors were a positive skin prick test and living with animals.

Discussion: The prevalence of wheeze in children in the Jimma region is low, particularly in rural children. In addition to having an impact on disease prevalence, place of residence also appears to modify the impact of environmental risk factors for wheeze.

Introduction

The asthma epidemics that have emerged in a number of European countries during the past four decades now appear to have peaked.^{1,2} This

suggests that within these countries all of the susceptible population has now been exposed to the relevant environmental causes, and this in turn

*Address correspondence to Dr R. Hubbard, University of Nottingham, Division of Respiratory Medicine, Clinical Sciences Building, Nottingham City Hospital, Nottingham NG5 1PB.
e-mail: Richard.Hubbard@nottingham.ac.uk*

QJM vol. 97 no. 8 © Association of Physicians 2004; all rights reserved.

makes these exposures difficult to identify. In other less developed areas of the world, however, asthma epidemics are just starting.³ In these populations, therefore, the opportunity to identify which environmental exposures initiate and drive asthma epidemics remains.

Studies of asthma epidemics have suggested that initially the epidemic starts in adults, and that the prevalence increases in children at a later stage.⁴ The reasons for this are not known. We have previously studied asthma in adults and older children in the Jimma region of Ethiopia. We found that the prevalence of asthma there is low compared to European levels, but is higher in older people compared to younger people, and in the urban compared to the rural setting.⁵ Similar findings have also been reported in other studies from Africa.^{6,7} Part of the urban/rural difference in prevalence in Jimma appears to be due to differences in parasite load,⁸ but other factors, such as allergen exposures⁸ and indoor pollution,⁹ may also have roles. To establish whether the asthma epidemic in Jimma also involves younger age groups, and whether the same environmental risk factors are relevant, we have completed a survey of younger children in the region. Our initial results have again shown that the presence and severity of parasitosis appears to have an impact on the risk of wheeze.¹⁰ In this paper, we examine the impact of other environmental exposures, including perinatal factors, indoor pollution and exposure to animals, on the risk of wheeze in the last year in young children in urban and rural communities in Jimma.

Methods

The methods for our cross-sectional survey have been described before in detail.¹⁰ Briefly, our study population consisted of all children aged 1–4 years living in Jimma town and three surrounding rural communities: Shebe, Agaro and Asendabo. This region is to the south-west of Addis Ababa, and since it has a regular rainy season, is considerably greener than the more Northern parts of Ethiopia. Trained fieldworkers conducted interviews with parents/guardians using a questionnaire based on the ISAAC study questionnaire,¹¹ which was translated into Ahmaric, and checked by back translation into English. The questionnaire also included questions on peri-natal factors, family size, maternal and paternal educational status (subsequently grouped according to the highest educational level of either parent as follows: illiterate, grade 1–6, grade 7–12, higher education), household exposures, fuel use and various other lifestyle factors.

The fieldworkers then carried out allergen skin tests to *D. pteronyssinus* and cockroach, with saline and histamine controls, on all children. A skin test was defined as positive if the mean wheal diameter was greater than the saline control diameter by 2 mm or more.

Our primary study outcome was parent-reported wheeze in the last 12 months. We assessed the impact of environmental exposures and the presence of a positive skin test on wheeze, by using logistic regression to model the impact of each variable in turn on a baseline model that included age and gender, our *a priori* confounders. Since our previous analysis had demonstrated that the results were markedly different for urban and rural children,¹⁰ we stratified all analyses according to urban/rural place of residence, and have presented results separately for urban and rural children, but where appropriate we have also carried out statistical tests for interaction using multiplicative interaction terms. Finally we constructed multivariate models including all exposures associated with wheeze in either the urban or rural children, and for simplicity sake we fitted all of these variables in the same final model for the urban and rural population. We used Stata (version 7) for all analyses.

Results

Survey population

A total of 7155 children took part in our survey. Since there are no accurate local census data, we cannot calculate a definitive response rate, but anecdotally, refusals were rare. Of the children taking part in the study, 3623 (51%) were female, and 4285 (60%) and 2870 (40%) lived in the urban and rural communities, respectively. The mean age of the children was 3 years (SD 1.1 years), although in most cases the age was interpolated from the year of birth, since the precise date of birth was not usually known. The prevalence of wheeze was 3.4%, and its distribution by age, sex and urban or rural area is shown in Table 1. Wheeze was marginally more common in boys ($p=0.08$), and tended to increase with increasing age (p for trend 0.051). After adjusting for the effects of age and gender, children living in the rural area had less than half the risk of urban children of having wheeze in the last year (OR 0.47, 95%CI 0.34–0.66, $p=0.0001$). The ORs for age and gender were similar when examined in the urban and rural populations separately.

Table 1 The prevalence of wheeze in the last year by demographic group

	Wheeze in the last year (<i>n</i> = 246)	No wheeze in the last year (<i>n</i> = 6909)	OR*	95%CI
<i>Gender</i>				
Girls	109 (3.0%)	3514 (97.0%)	1	
Boys	137 (3.9%)	3395 (96.1%)	1.27	0.97–1.67 <i>p</i> = 0.08
<i>Age (years)</i>				
1	23 (2.8%)	804 (97.2%)	1	
2	61 (3.4%)	1721 (96.6%)	1.23	0.76–2.01
3	49 (3.0%)	1592 (97.0%)	1.07	0.65–1.77
4	64 (3.8%)	1614 (96.2%)	1.38	0.85–2.24
5	20 (5.4%)	351 (94.6%)	2.01	1.09–3.70 <i>p</i> _{trend} = 0.051
<i>Location</i>				
Urban	188 (4.4%)	4097 (95.6%)	1	
Rural	58 (2.0%)	2812 (98%)	0.47	0.34–0.66 <i>p</i> = 0.0001

*Odds ratios adjusted for age and sex

Table 2 The relation between the presence skin sensitization and wheeze in the last year

Allergen	Urban children				Rural children			
	Wheeze in last 12 months	No wheeze	OR*	95%CI	Wheeze in last 12 months	No wheeze	OR*	95%CI
House dust mite	3 (1.6%)	48 (1.2%)	0.97	0.23–4.03 <i>p</i> = 0.96	11 (19.0%)	211 (7.5%)	2.79	1.32–5.88 <i>p</i> = 0.015
Cockroach	6 (3.2%)	148 (3.6%)	0.78	0.32–1.94 <i>p</i> = 0.58	14 (24.1%)	252 (9.0%)	3.53	1.79–6.94 <i>p</i> = 0.001
Either	8 (4.3%)	181 (4.4%)	0.89	0.41–1.93 <i>p</i> = 0.76	20 (34.5%)	408 (14.5%)	3.01	1.62–5.59 <i>p</i> = 0.001

*Odds ratios adjusted for age and sex

Role of skin sensitization (Table 2)

A total of 617 (8.6%) children had a positive skin test to either *D. pteronyssinus* (house dust mite) or cockroach, and sensitization to cockroach allergen was more common than sensitisation to *D. pteronyssinus* (5.9% vs. 3.8%, *p* < 0.001). The prevalence of a positive skin test to either house dust mite or cockroach was higher in the rural than in the urban area (14.9% vs. 4.4%, *p* < 0.001, Table 2). In the rural area, the presence of a positive skin test to either house dust mite or cockroach was associated with wheeze, but this was not true in the urban area and this effect modification

was statistically significant (*p*_{interaction} = 0.013, Table 2).

Peri-natal factors (Table 3)

We found no evidence of an association between maternal age and risk of wheeze in either the rural or urban children (Table 3). In the rural areas, few parents had more than 6 years of schooling, and so we were unable to assess in detail the impact of this measure of socio-economic disadvantage on the prevalence of asthma. In the urban areas, the prevalence of wheeze did appear to increase with increasing parental educational level, but

Table 3 Impact of peri-natal factors on the risk of wheeze in the last year

Exposure	Urban children				Rural children			
	Wheeze in last year	No wheeze	OR*	95%CI	Wheeze in last year	No wheeze	OR*	95%CI
<i>Maternal age</i>								
≤22 years	72 (5%)	1351 (95%)	1		18 (2%)	949 (98%)	1	
23–28 years	64 (4%)	1614 (96%)	0.72	0.50–1.04	20 (2%)	1034 (98%)	1.06	0.52–2.17
≥29 years	52 (4%)	1114 (95%)	0.85	0.58–1.25 $p_{\text{trend}} = 0.34$	20 (2%)	823 (98%)	1.22	0.59–2.52 $p_{\text{trend}} = 0.6$
<i>Parental education level</i>								
1	7 (5%)	150 (95%)	1		26 (2%)	1531 (98%)		
2	39 (4)	946 (96%)	1.45	0.44–4.83	29 (3%)	993 (97%)	1.60	0.88–2.89
3	105 (5%)	2210 (95%)	1.86	0.58–5.97	3 (1%)	271 (99%)	0.53	0.12–2.56
4	37 (5%)	788 (95%)	1.78	0.54–5.91 $p_{\text{trend}} = 0.24$	0	17 (100%)		$p_{\text{trend}} = 0.9$
<i>Duration of breastfeeding</i>								
0–12 months	58 (3%)	1616 (97%)	1		17 (3%)	582 (97%)	1	
13–24 months	83 (5%)	1756 (95%)	1.40	0.97–2.00	27 (2%)	1760 (98%)	0.51	0.24–1.06
>24 months	47 (6%)	725 (94%)	1.76	1.15–2.71 $p_{\text{trend}} = 0.008$	14 (3%)	470 (97%)	1.03	0.43–2.46 $p_{\text{trend}} = 0.88$

*Odds ratio adjusted for age and sex

Table 4 Impact of cooking fuel on wheeze in the past year

Exposure to cooking fuel	Urban children			Rural children		
	Wheeze in last year	No wheeze	OR*	95%CI	Wheeze in last year	No wheeze
<i>Charcoal</i>						
Never	6 (3%)	225 (97%)	1		55 (2%)	2650 (98%)
Sometimes	32 (5%)	611 (95%)	2.73	0.82–9.16	3 (2%)	129 (98%)
Everyday	150 (4%)	3261 (96%)	2.72	0.86–8.64	0	33 (100%)
				$p_{\text{trend}} = 0.19$		
<i>Wood</i>						
Never	2 (4%)	52 (96%)	1		2 (2%)	107 (98%)
Sometimes	124 (4%)	2927 (96%)	0.93	0.22–3.88	0	12 (100%)
Everyday	62 (5%)	1118 (95%)	1.10	0.26–4.68	56 (2%)	2693 (98%)
				$p_{\text{trend}} = 0.6$		
<i>Kerosene</i>						
Never	122 (4%)	3040 (96%)	1		57 (2%)	2797 (98%)
Sometimes	54 (5%)	958 (95%)	1.39	0.98–1.96	1 (7%)	14 (93%)
Everyday	12 (11%)	99 (89%)	3.34	1.78–6.29	0	1
				$p_{\text{trend}} = 0.001$		
<i>Electricity</i>						
Never	172 (4%)	3799 (96%)	1		58 (2%)	2811 (98%)
Sometimes	13 (4%)	279 (96%)	1.03	0.56–1.87	0	1
Everyday	3 (14%)	19 (86%)	3.68	1.07–12.6		
				$p_{\text{trend}} = 0.25$		

*Odds ratio adjusted for age and sex

Insufficient data

Insufficient data

0.23–4.08
–
 $p_{\text{trend}} = 0.63$ 0.18–3.21
 $p_{\text{trend}} = 0.77$

Table 5 Impact of environmental tobacco smoke on wheeze in the last year

Exposure	Urban children				Rural children			
	Wheeze in last year	No wheeze	OR*	95%CI	Wheeze in last year	No wheeze	OR*	95%CI
<i>Any smoker in the home</i>								
No	151 (4%)	3576 (96%)	1		34 (2%)	2051 (98%)	1	
Yes	37 (7%)	521 (93%)	1.82	1.24–2.68 $p=0.004$	24 (3%)	761 (97%)	1.63	0.89–2.98 $p=0.12$
<i>Cigarettes in the home per day</i>								
0	151 (4%)	3576 (96%)	1		34 (2%)	2051 (98%)	1	
1–9	19 (7%)	265 (93%)	1.89	1.13–3.14	19 (4%)	509 (96%)	1.94	1.00–3.75
10–19	8 (5%)	163 (95%)	1.19	0.55–2.59	3 (1%)	229 (99%)	0.59	0.14–2.48
20+	10 (10%)	92 (90%)	2.71	1.38–5.34 $p_{\text{trend}}=0.002$	2 (8%)	23 (92%)	6.42	1.42–29.0 $p_{\text{trend}}=0.18$

*Odds ratio adjusted for age and sex

this trend was not statistically significant. Most children were breast-fed for >12 months in both urban and rural areas. In the urban area, the risk of wheeze in the last year increased with increasing duration of breastfeeding, but no clear trend was present in the rural area. The test of interaction for the difference in impact of breastfeeding duration on wheeze in the urban and rural setting was on the borderline of statistical significance ($p_{\text{interaction}}=0.06$). We found no evidence to suggest that season of birth or birth order had any impact on the risk of wheeze in either area, and there were insufficient data to assess the impact of birth weight.

Indoor pollution, house constitution and bedding materials (Tables 4 and 5)

In the rural region, the use of wood as a fuel was almost universal, while use of other fuel sources was rare (Table 4). In the urban area, however, there was more diversity of fuel use, and most households reported using charcoal ($n=4054$, 95%), some used kerosene ($n=1123$, 26%), and a few used electricity ($n=314$, 10%). In the urban setting, the daily use of fuels other than wood did appear to be associated with an increased risk of wheeze, but overall a statistically significant association was only present for exposure to kerosene (Table 4). The use of kerosene was also associated with parental educational level, but adjustment for this variable had little effect on the ORs for the daily use of kerosene (adjusted OR 3.38, 95%CI 1.77–6.47, overall $p_{\text{trend}}=0.001$).

The proportion of homes with a current smoker was higher in the rural than in the urban area

(27% vs. 13%), and in both settings, the presence of a smoker appeared to increase the risk of wheeze (Table 5). The OR was smaller in the rural area, however, and the CIs included unity, but there was no evidence of significant interaction ($p_{\text{interaction}}=0.8$). There was evidence of a dose-response relationship between environmental tobacco smoke and wheeze in the urban area ($p_{\text{trend}}=0.002$), but this relationship was less clear in the rural setting ($p_{\text{trend}}=0.18$).

Additional housing factors, such as the material used to build the house and the nature of the bedding did not have any effect on the risk of wheeze in the last year.

Exposure to animals and farming (Table 6)

Children living in the rural area were slightly more likely to report living with animals than those in the urban area (81% vs. 73%), and tended to live with a larger number of species (median number of species 2 vs. 1). In the rural area, exposure to all species of animal appeared to be associated with an increased risk of recent wheeze, and this effect was particularly marked for living with a cat (Table 6). In addition, there was an exposure-response relationship present between the number of species and the risk of having wheeze in the last year ($p_{\text{trend}}=0.033$). In contrast, in the urban area, living with animals appeared to be associated with a reduced risk of wheeze in the last year, and this difference between the urban and rural setting was statistically significant ($p_{\text{interaction}}=0.04$). In addition, in the urban setting, the number of different species appeared to provide a dose-related protective effect ($p_{\text{trend}}=0.001$, Table 6).

Table 6 Impact of living with animals on wheeze in the last year

Exposure	Urban children				Rural children			
	Wheeze in last year	No wheeze	OR*	95%CI	Wheeze in last year	No wheeze	OR*	95%CI
Living with any animal	116 (4%)	2993 (95%)	0.61	0.44–0.83 $p=0.003$	48 (2%)	2269 (98%)	1.50	0.63–3.56 $p=0.94$
Sheep	4 (2%)	171 (98%)	0.43	0.13–1.37	19 (3%)	649 (97%)	1.95	1.08–3.54
Hen	80 (4%)	2003 (94%)	0.79	0.58–1.08	34 (2%)	1526 (98%)	1.25	0.69–2.25
Cow	17 (3%)	519 (97%)	0.63	0.36–1.10	40 (2%)	1857 (98%)	1.23	0.64–2.34
Cat	65 (4%)	1627 (96%)	0.80	0.58–1.11	13 (3%)	370 (97%)	2.19	1.12–4.26
Dog	52 (3%)	1625 (97%)	0.60	0.43–0.85	4 (2%)	170 (98%)	1.42	0.50–4.03
OR per additional species			0.79	0.69–0.91 $p_{\text{trend}}=0.001$			1.37	1.03–1.84 $p_{\text{trend}}=0.033$

*Odds ratio adjusted for age and sex

Table 7 Multivariate analysis

Exposure	Urban children		Rural children	
	OR	95%CI	OR	95%CI
Any positive skin test	0.93	0.43–2.02 $p=0.86$	2.94	1.57–5.50 $p=0.001$
<i>Duration of breastfeeding</i>				
0–12 months	1		1	
13–24 months	1.39	0.97–2.00	0.51	0.24–1.06
>24 months	1.70	1.10–2.62 $p_{\text{trend}}=0.014$	0.99	0.41–2.40 $p_{\text{trend}}=0.96$
<i>Use of kerosene</i>				
Never	1		Insufficient data	
Sometimes	1.44	1.02–2.05		
Daily	3.36	1.77–6.36 $p_{\text{trend}}=0.001$		
Any smoker in the house	1.81	1.23–2.67 $p=0.003$	1.66	0.90–3.05 $p=0.1$
Living with animals	0.82	0.71–0.94 $p=0.005$	1.40	1.04–1.87 $p=0.03$

Multivariate analysis (Table 7)

The results of the multivariate analyses are shown in Table 7. Combining the variables together had little impact on any of the ORs for either the rural or the urban model.

Discussion

Our study demonstrates that young children living in the Jimma region of Ethiopia have a low prevalence of wheeze, compared to children living in the UK and other developed countries.¹¹ This is particularly true for children living in rural commu-

nities, where the prevalence of wheeze was only 2%, and was half that found in children living in the urban community. In addition to its impact on wheeze prevalence, urban or rural residence also appeared to modify the relation between having a positive skin test and wheeze, such that for children living in the rural region the presence of positive skin tests was a risk factor for wheeze, while for children living in the urban region there was no association. Place of residence also appeared to modify the impact of duration of breastfeeding and close exposure to animals on the risk of wheeze. In the urban area, a longer duration of breastfeeding was a risk factor for wheeze, but this was not true in the rural area, and while exposure to animals

appeared to reduce the risk of wheeze in urban children, the opposite was true in rural children. Children living in the urban area were exposed to more non-wood fuels, and in particular, regular exposure to kerosene appeared to be an important risk factor for wheeze, independent of parental educational status. Since exposure to kerosene was virtually absent in the rural communities, this exposure may explain in part the higher levels of wheeze in the urban setting.

Our findings are consistent with a number of studies of asthma in African populations^{5-7,11-13} in showing that at the present time, the prevalence of wheeze is low in Africa in comparison to European, North American and Australasian populations, but that within African populations, wheeze is more common in urban populations. Our study is one of the first to focus on wheezing illness in young African children, however, and to demonstrate the emergence of wheeze as a health problem in this age group. In our study we defined asthma on the basis of responses to the ISAAC question on recent wheeze. This question has been used before in Ethiopia and other African countries, and appears to have good validity in older children in these populations.¹¹ We did not specifically test its validity in younger children. We attempted to study all the children living within the defined rural and urban areas, and anecdotally refusals to take part in the study were rare. We therefore believe that significant selection or information biases in our data are unlikely. There are other weaknesses in our study, however, which relate to its cross-sectional design and the practical difficulties of collecting data on some exposures. For example, we were not able to divide the children with wheeze into those with transient as opposed to persistent illness, to study the impact of environmental exposure on different asthma phenotypes. We did not collect detailed information on early-life illnesses such as episodes of diarrhoea and/or pneumonia, and we did not have the financial resources to collect detailed anthropometric data.

We found that wheeze was marginally more common amongst young boys compared to young girls, and this finding is consistent with a number of other studies in Europe.^{14,15} One proposed explanation for this finding is the smaller airway calibre in boys, although there are data to suggest that the prevalence of other allergic diseases is higher in young boys than in young girls.¹⁴ We found no clear impact of age on the risk of wheeze, though this may be due in part to the narrow age range studied and the inaccuracy of ascertainment of age in children in these populations.

Consistent with our studies in adults, the presence of a positive skin test to common aeroallergens was more common in the rural population than the urban population.⁵ The prevalence of positive skin tests in young urban children was similar to that seen in data from Europe,¹⁶ while the levels present in the rural districts were considerably higher, and the reasons for this are unclear. Importantly, however, the relation between the presence of a positive skin test and recent wheeze in the current study differs to that in our previous study of adults.⁵ In adults, the presence of a positive skin test appeared to reduce the risk of wheeze in the rural populations and increase the risk of wheeze in the urban populations. In our current study in children the opposite was true, and in rural children a positive skin test was a risk factor for wheeze, with no relationship apparent in the urban population. The reasons for this are not clear, and we cannot exclude the possibility that this is a chance finding. An alternative explanation, however, is that in evolutionary terms the rural population in Jimma represent the normal human 'wild type', and that the development of sensitization to common aeroallergens and its transient association with allergic disease is part of normal development. Some parallels may be drawn with the development of sensitization to food allergens early in life in European children, and the role of this as a risk factor for eczema, which for most children is a transient illness.¹⁷ To answer this question definitively, a cohort study is required in which skin sensitization and allergic disease is studied in both the urban and rural children prospectively from birth.

We found no impact of maternal age on wheeze in either population, and this finding contrasts with data from Europe.^{14,18} Since accurate estimate of maternal age is a particular problem in this population, random misclassification of maternal age may have had an important role in removing this effect. The duration of breastfeeding present in both urban and rural communities is far greater than that seen in European populations, and interestingly, children that were breast-fed for more than one year were at increased risk of wheeze in the urban area. Although this may reflect a direct adverse effect of prolonged breastfeeding, it may also be that longer duration of breastfeeding is associated with poverty and poorer diet in general in children and mothers, and that it is these confounding variables that explain the association with wheeze. In addition, it is possible that mothers will breastfeed children who have had wheezing during infancy for longer periods of time because they perceive them to be weak and in need of more nutrition. The uniformly

low socio-economic status and lack of non-wood fuel use in the rural areas meant we could not study these factors in that population, but in the urban setting the use of kerosene was associated with an increased risk of wheeze, and this finding is consistent with our study in adults, which found that the use of kerosene was a risk factor for wheeze.⁹ An alternative explanation is that these findings reflect, at least in part, an impact of higher socioeconomic on wheezing illness in urban children. This seems unlikely, however, because socio-economic status was not a strong risk factor for asthma in our dataset, and adjusting our models for parental educational status had little impact on these findings. In addition, we did have more detailed information on paternal occupation, but again adjusting our models for this additional marker of socio-economic status did not attenuate the influence of kerosene.

Cigarette smoking is becoming more prevalent in Ethiopia, and our findings of an impact of environmental tobacco smoke on wheezing illness in younger children are therefore not surprising.¹⁹ In rural areas, people tend to smoke hand-rolled cigarettes containing locally grown tobacco and other plants, while in the urban setting, people are increasingly smoking manufactured cigarettes. It is possible that the different types of cigarette consumed in the two populations explain why environmental tobacco smoke appears to be marginally more harmful in the urban setting.

In the urban community, animal ownership was associated with a decreased prevalence of wheeze, and this finding is consistent with an increasing evidence emerging from Europe that exposure to farm animals may have a protective role.²⁰ In contrast, in the rural setting, living with animals increased the risk of wheezing illness. The reasons for this are not clear, but children living in the rural area tend to live with more animals, both in terms of numbers and species, and anecdotally they appear to have much more contact with their animals and live much closer to them. It is possible that living in this way this leads to much higher levels of lipopolysaccharide exposure, and that this high level of exposure leads to airway inflammation and wheeze rather than exerting a protective influence.²¹

In summary, asthma is emerging as a public health problem in children in Jimma. At present the children at greatest risk are those living in the urban communities, who are breast-fed for longer and exposed to environmental tobacco smoke and kerosene. In contrast to our previous study in adults, skin sensitization in rural children appears to be a risk factor for wheeze, suggesting that the natural history of allergic sensitization and its rela-

tion with allergic disease differs in the urban and rural communities. A prospective birth cohort study of these phenomena would be helpful in establishing clearly the temporal relationship between the development of skin sensitization and the clinical manifestations of allergic disease.

Acknowledgements

This study was funded by The Wellcome Trust.

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