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Characterisation of asthma among adults with and without childhood farm contact

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ABSTRACT: Childhood farm contact is associated with a lower prevalence of sensitisation and allergic rhinitis. Findings have been contradictory for asthma. The aim of the present study was to investigate the differences between farm and nonfarm subjects using objective measurements.

A cross-sectional questionnaire study was performed among rural adults aged 18–44 yrs, of which 37% lived on a farm during the first 3 yrs of life and were thus referred to as "farm subjects". Lung function, bronchial hyperresponsiveness (BHR) to methacholine and sensitisation were measured in a random sample. A total of 1,595 subjects were included in the analyses.

Among farm subjects, sensitisation against inhalant allergens (odds ratio (OR) 0.7; 95% confidence interval 0.6–0.9), allergic rhinitis (0.5 (0.4–0.8)) and asthma diagnosis (0.7(0.4–1.1)) were less common than among nonfarm subjects. For BHR and lung function, no statistically significant differences were found between the two groups. Stratifying for sensitisation, farm subjects had a lower OR of asthma diagnosis (0.5 (0.3–1.0)) and a nonsignificantly reduced OR of BHR with sensitisation (0.8 (0.5–1.1)).

The present study confirmed, using objective measurements, that farm subjects have a lower prevalence of symptoms and asthma diagnosis, while the prevalence of bronchial hyperresponsiveness does not differ.

KEYWORDS: **Bronchial provocation, farming, hygiene hypothesis, inhalant allergens, lung function tests**

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STATEMENT OF INTEREST
None declared.

It has been suggested that a more hygienic lifestyle may be responsible for the increase in allergic disease in recent years [1]. Several studies [2–6] have shown that growing up on a farm is associated with a lower prevalence of sensitisation and hay fever among children, a fact that backs up the hygiene hypothesis. Different studies [7–11] have suggested that the effect of childhood farm living on sensitisation and hay fever may persist until adulthood.

Some studies [5–7, 10, 12] also showed a lower prevalence of asthma and asthma-like symptoms for individuals who lived on a farm during childhood. However, other studies showed heterogeneous effects across different study centres [13] or for different timing of farm living [14]. In some cases [15], farm living even tended to be a risk factor for asthma.

It is possible that a different aetiology of allergic and nonallergic asthma may help explain the aforementioned findings [16]. Although asthma is still widely thought to be an atopic disease, usually less than half of adult asthmatics are atopic [17]. Therefore, the influence of testing for sensitisation on asthma diagnosis should not be underestimated.

Another problem may be the different definitions of asthma encountered across studies due to the lack of a gold standard. A highly sensitive but less specific definition of asthma includes the test for bronchial hyperresponsiveness (BHR) [18]. The specificity might be increased using self-reported doctors' diagnosed asthma; however, variations in awareness of asthma symptoms and thus use of health services, as well as labelling of asthma by doctors, might reduce the validity of the definition [19].

The aim of the present study was to investigate the differences in asthma and allergies between rural farm and nonfarm subjects using questionnaire data and objective measurements. Different phenotypes of asthma, as well as differences in perception of asthma symptoms, between farm and nonfarm subjects were assessed.

METHODS

Study design and data collection

Through local registration authorities, all adults of German nationality aged 18–44 yrs, who lived in four selected rural towns in Lower Saxony (North-Western Germany), were asked to take part in the Lower Saxony Lung Study. Before

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mailing the questionnaire, subjects were randomly divided in two groups (fig. 1). The first group was asked to join the questionnaire survey and the medical examination (n=7,080), while the second group was asked to join the questionnaire survey only (n=3,172). Subjects received the questionnaire and a letter between 2002 and 2004 explaining the study. Where necessary, repeated contacts ensued in order to secure maximum response. Questionnaire participation was 67% in the group with medical examination and 70% in the group with questionnaire only. The study was approved by the Medical Ethical Committee of the Ludwig-Maximilians-University Munich (Munich, Germany) and the Lower Saxony Medical Board.

Respiratory health questions were taken from the European Community Respiratory Health Survey questionnaire [20]. Data on specific farm-related items were obtained using questions taken from the Allergy and Endotoxin study [2]. In addition, questions on demographic characteristics and other potential confounders were asked.

Medical examination consisted of pulmonary function testing, followed by bronchial challenge with methacholine (MCH) and blood sampling. Informed consent for the medical examination was obtained from 2,812 of the eligible subjects (40% of those invited by questionnaire). Figure 1 shows the number of subjects completing the separate parts of the medical examination. Exclusion criteria for the MCH challenge (*e.g.* heart disease, pregnancy, forced expiratory volume in one second (FEV_1) <80% predicted) accounted for 59% of the subjects not tested for BHR. Participants of the MCH challenge were more likely to be male and less likely to have symptoms of asthma than nonparticipants. After a detailed explanation of

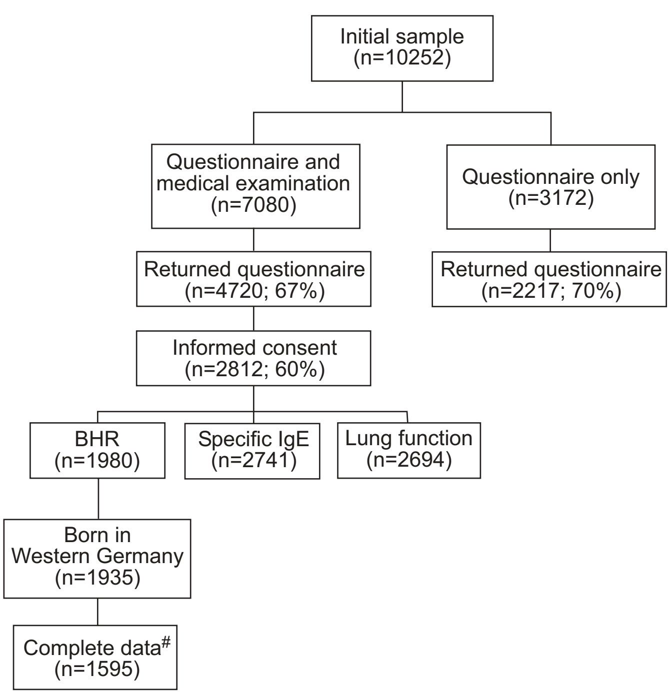

FIGURE 1. Flow chart of the study and subjects included in the present analyses. BHR: bronchial hyperresponsiveness; Ig: Immunoglobulin. #: subjects included in the present analyses.

the procedure, 23% refused to cooperate and the remaining 18% gave no reason for not cooperating.

Lung function was performed with a body plethysmograph (Jaeger, Würzburg, Germany), according to American Thoracic Society criteria [21], and is shown as percentage of predicted, based on sex, height and age [22]. The Tiffeneau index was calculated as the ratio of FEV_1 and vital capacity [22]. In addition, the MCH challenge was performed stepwise (doubling or quadrupling doses), using an APS dosimeter (Jaeger) until a fall in FEV_1 of 20% occurred (maximum cumulative dose 1.2 mg). The procedure was adapted from the European Community Respiratory Health protocol. As previously described elsewhere [23], the number of false positives at a cumulative dose of 1.2 mg was high. Therefore, a cumulative dose of 0.6 mg was chosen as a cut-off value for the analyses. However, using 1.2 mg as a cut-off level did not considerably change the results.

Specific immunoglobulin (Ig)E was measured in serum samples (Pharmacia, Freiburg, Germany) against a mix of inhalant allergens (*via* SX1 allergy screening; Timothy grass, rye, mugwort, birch, *Dermatophagoides pteronyssinus*, *Cladosporium herbarum*, cat and dog). A specific IgE concentration of 0.35 $kU \cdot L^{-1}$, corresponding to a radioallergosorbent test class $\geqslant$1, was regarded as positive [20].

Statistical methods

Logistic regression analysis was used to calculate odds ratios (OR) with 95% confidence interval (CI). These models were *a priori* adjusted for sex, age, passive and active smoking, level of education, family history of allergic disease and number of siblings.

Linear regression analysis was used to calculate differences in lung function parameters between different groups.

RESULTS

The statistical analyses were based upon subjects with complete data who were born in the former Western part of Germany (n=1,595; fig. 1). Subjects included in the analyses were more likely to have lived on a farm during the first 3 yrs of life. These were referred to as ''farm subjects''. Subjects included in the analyses were older and less likely to be active smokers than subjects excluded from the analyses. In addition, subjects included in the analyses reported symptoms of wheezing without having a cold or an asthma diagnosis less frequently (table 1).

The prevalence of allergic rhinitis and sensitisation among farm subjects was about half of the prevalence among the nonfarm population (table 2). Similar results were seen for doctors' diagnosis of asthma and wheezing. Stratifying for sensitisation the differences in asthma diagnosis between the two groups were confined to sensitised subjects. However, CIs overlapped and the interaction term between sensitisation and farm contact did not reach the level of statistical significance (p=0.56). BHR and baseline Tiffeneau index were not significantly different between farm and nonfarm subjects. The same was true for other lung function parameters (data not shown). Similar results were seen when adjusting for potential confounders.

TABLE 1 Descriptive data comparing subjects# included in the analyses with those who had to be excluded

	Included	Excluded
Subjects n	1595	4358
Farm living during childhood**	677 (42.5)	1539 (35.6)
Female sex	818 (51.3)	2158 (49.5)
Age yrs**		
18–25	249 (15.6)	977 (22.4)
26–30	218 (13.7)	595 (13.7)
31–35	339 (21.3)	904 (20.7)
36–40	447 (28.0)	1066 (24.5)
41–44	342 (21.4)	816 (18.7)
Active and passive smoke exposure**		
Not at all	508 (31.9)	1199 (28.1)
Only ETS	206 (12.9)	569 (13.3)
Ex-smoker	345 (21.6)	856 (20.1)
Current smoker	536 (33.6)	1640 (38.5)
Education >12 yrs	399 (25.0)	1064 (24.9)
Family history of allergic disease	534 (33.5)	1176 (31.4)
No. of siblings ⩾3	851 (53.4)	2171 (51.2)
Wheezing without a cold**	167 (10.5)	564 (13.0)
Allergic rhinitis	231 (14.5)	569 (13.3)
Asthma diagnosis**	79 (5.0)	297 (6.9)

Data are presented as n (%), unless otherwise stated. ETS: environmental tobacco smoke. #: born in the former Western part of Germany (n=5,953); **: p<0.01 (Chi-squared test).

To further study the protective influence of a farm childhood on asthma phenotype, the overlap between asthma diagnosis, BHR and sensitisation for farm and nonfarm subjects was analysed (fig. 2). In these analyses the adjusted ORs for farm, as compared with nonfarm subjects, were less than one for combinations involving sensitisation only.

DISCUSSION

The comparison between rural subjects who grew up on a farm and rural subjects without a farm childhood resulted in a significantly lower prevalence of allergic rhinitis, sensitisation and asthma, but not BHR or lung function for farm subjects.

Different papers investigating the effect of a farm childhood on respiratory health of adults are available. In these studies [7, 10, 12, 24, 25] a lower prevalence of allergies could be confirmed, while the results on the prevalence of asthma have been conflicting. Different asthma phenotypes between farm and nonfarm subjects have been discussed in this context. EDUARD *et al.* [24] showed a lower prevalence of atopic and a higher prevalence of nonatopic asthma comparing animal farmers with farmers producing plants. These results could not be confirmed when comparing farmers with the general population [25]. One reason might be that current exposure to the farming environment, and not childhood exposure to the farming environment, was used as marker of exposure in the study by EDUARD *et al.* [25].

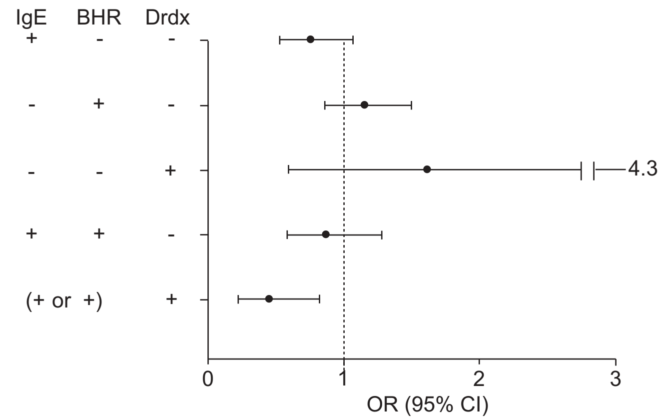

FIGURE 2. Adjusted odds ratio (OR; 95% confidence interval (CI)) of immunoglobulin (Ig)E, bronchial hyperresponsiveness (BHR) and asthma diagnosis (Drdx) and their combination for farm subjects (n=537) when compared with nonfarm subjects (n=653). A specific IgE concentration of 0.35 $kU \cdot L^{-1}$, corresponding to a radioallergosorbent test class ⩾1, was regarded as positive. Adjusted for sex, age, passive and active smoke exposure, level of education, family history of allergic diseases and presence of siblings.

In the present study, approximately one-third of the farm subjects also had current farm contact. Therefore, one might speculate that the associations seen were mainly driven by current farm contact, rather than by childhood farm living. However, taking current exposure during adulthood into account did not change the present results. Likewise, restricting the current study population to subjects with farm contact during the first 3 yrs of life and those who never had farm contact did not alter the findings. Unfortunately, intensity of recent farm contact could not be included in the analyses as the data were not available for the participants.

With respect to living on a farm in early childhood, the present authors had to rely on self-reports. Therefore, some misclassification of exposure may bias the results. Furthermore, migration out of the study area might have occurred. As the likelihood of migration might be related to both exposure and outcome, this might have biased the present results. Only prospective cohort studies starting in early childhood may overcome this problem.

The strengths of the present study were: 1) a good response to the questionnaire part of the study among a large population-based sample of rural subjects; 2) the use of validated questionnaire instruments [23]; and 3) objective measurements of sensitisation, lung function and BHR in approximately half of the population. To reduce selection bias, subjects were *a priori* randomly divided in two groups. The first group was asked to join the questionnaire survey and the medical examination, while the second group was asked to join the questionnaire survey only. The clinical measurements were performed according to standardised procedures with thorough quality control.

A considerable proportion of subjects were not tested for BHR, which could have introduced some selection bias. As the proportion of asthmatics was the same among the individuals who participated in the clinical measurements (6.1%) and those

TABLE 2 Prevalence and odds ratios (OR) comparing farm[#] and nonfarm[¶] subjects for respiratory symptoms, asthma and allergic rhinitis, sensitisation, bronchial hyperresponsiveness (BHR) and lung function

	Subjects n	Prevalence	OR (95% CI)	
			Unadjusted	Adjusted
Allergic rhinitis				
Nonfarm	918	167 (18.2)	1	1
Farm	677	64 (9.5)	0.47 (0.35–0.64)	0.54 (0.39–0.75)
Sensitisation SX1 >0.35				
Nonfarm	918	250 (27.2)	1	1
Farm	677	130 (19.2)	0.64 (0.50–0.81)	0.73 (0.57–0.94)
Wheezing without a cold				
Nonfarm	918	111 (12.1)	1	1
Farm	677	56 (8.3)	0.66 (0.47–0.92)	0.73 (0.51–1.04)
With sensitisation				
Nonfarm	854	47 (5.5)	1	1
Farm	643	22 (3.4)	0.61 (0.36–1.02)	0.72 (0.42–1.23)
Without sensitisation				
Nonfarm	871	64 (7.4)	1	1
Farm	655	34 (5.2)	0.69 (0.45–1.06)	0.73 (0.46–1.15)
Asthma diagnosis[+]				
Nonfarm	918	56 (6.1)	1	1
Farm	677	23 (3.4)	0.54 (0.33–0.89)	0.65 (0.39–1.08)
With sensitisation				
Nonfarm	903	41 (4.5)	1	1
Farm	667	13 (2.0)	0.42 (0.22–0.79)	0.50 (0.26–0.96)
Without sensitisation				
Nonfarm	877	15 (1.7)	1	1
Farm	664	10 (1.5)	0.88 (0.39–1.97)	1.05 (0.46–2.43)
BHR[§]				
Nonfarm	918	308 (33.6)	1	1
Farm	677	211 (31.2)	0.90 (0.73–1.11)	1.01 (0.81–1.27)
With sensitisation				
Nonfarm	731	121 (16.6)	1	1
Farm	524	58 (11.1)	0.63 (0.45–0.88)	0.77 (0.54–1.10)
Without sensitisation				
Nonfarm	797	187 (23.5)	1	1
Farm	619	153 (24.7)	1.07 (0.84–1.37)	1.15 (0.88–1.49)
Lung function				
Tiffeneau index % pred				
Nonfarm	915	99.9 (0.24)	0	0
Farm	673	99.7 (0.26)	-0.20 (-0.91–0.50)	-0.21 (-0.93–0.51)

Data are presented as n or n (%), with the exception of lung function which is presented as % (SE) and unadjusted and adjusted mean difference (95% CI). SX1: an allergy screening test; % pred: % predicted. #: lived on a farm in the first 3 yrs of life; ¶: did not live on a farm in the first 3 yrs of life; +: ever diagnosed by a physician; §: defined by a decrease in forced expiratory volume in one second >20% after methacholine challenge (⩽0.6 mg). ORs are shown unadjusted and adjusted for sex, age, passive and active smoke exposure, education level, family history of allergic disease and presence of siblings.

who did not (5.7%; p=0.70), no major bias was anticipated. The percentage of farm (3.8%) and nonfarm subjects (5.2%) that had to be excluded from the bronchial challenge due to low baseline FEV1 values differed slightly but it was not statistically significant (p=0.10, Chi-squared test).

As no gold standard for asthma exists [18, 19], asthma was defined in several different ways in the present study. However, the results were similar irrespectively of the definition used, *e.g.* asthma diagnosis, symptoms of wheeze without having a cold. In addition, defining asthma as having an asthma attack, having been woken by an attack of shortness of breath during the previous 12 months or currently taking asthma medication (current asthma), as suggested by KOGEVINAS *et al.* [26], did not alter the results.

In conclusion, the present study demonstrates that adult subjects who grew up on a farm exhibit a lower prevalence of respiratory allergies and report asthma symptoms and diagnosis less frequently. However, no differences between farm and nonfarm subjects could be found in the prevalence of bronchial hyperresponsiveness.

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