

The prevalence of atopic dermatitis in children is influenced by their parents' education: results of two cross-sectional studies conducted in Upper Austria

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Atopic dermatitis (AD) is an important health problem worldwide. Several studies have shown that a positive family history is a strong risk factor. We studied the prevalence of AD among 23,583 Austrian school children and examined the association between the prevalence of AD in children and their parents' education at two points in time. As part of the International Study of Asthma and Allergy in Childhood programme, two cross-sectional studies were conducted in Upper Austria (Federal State of Austria) between the years 1995–97 (Phase I) and 2001–03 (Phase III). All pupils of pre-school classes and of first and second grade of all elementary schools in seven districts of Upper Austria received standardized questionnaires, resulting in a total of 13,399 (Phase I) and 13,731 (Phase III) children. All variables examined concerning AD showed an increase in prevalence in the age group examined: During the first study, 9.6% of the children ever had eczema diagnosed by a doctor (Phase III: 13.3%), whereas 9.2% ever had symptoms of AD (Phase III: 11.0%). In Phase I, 6.0% of the children had an itchy rash in the past 12 months (Phase III: 6.7%). In both studies, high parental education (i.e. high school or university degree) was an independent statistically significant risk factor for eczema in the child, resulting in an adjusted Odds Ratio between 1.13 and 1.37. In a census-like-survey, we are able to demonstrate a statistically significant association between parental education and the prevalence of AD in their children, which is independent of a possible parental AD.

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We report about the examination of the association between parental education and atopic dermatitis (AD, synonym eczema) at two points in time. AD is a health problem worldwide. As there are considerable differences in prevalence between and within countries, 5–20% of the children aged between 6 and 14 are affected by this disease (1). In most cases, AD emerges in the first months of life, while its prevalence decreases by age (2–4). In the last couple of years, evidence grew that girls more often suffer from AD than boys (1, 5–8), but Verboom et al. showed that until the age of 6, both sexes are affected equally

(9). From this age on, the prevalence of AD in girls increases stronger than in boys (10). About 40% of the children affected still suffer from the disease in adulthood (11).

The prevalence rates vary substantially in different areas of the world (1, 12). Whereas in countries like Sweden, Japan, New Zealand, United Kingdom, Portugal and Thailand, a high prevalence of AD is found, Iran, Albania, India, Singapore and Spain are among the countries with the lowest prevalence rates (1). Globally, over time, most countries show an increase in the prevalence of AD (13).

A positive family history is a strong predictor of the development of AD in children (7, 14–20). However, as the prevalence rates change dramatically in some countries even in ethnically similar groups, gene variations cannot solely be made responsible for this outcome. Instead, a complex interaction of genes with environmental factors is considered to be liable (1, 6, 13, 21–23). Environmental factors seem to vary in different regions of the world (1). As AD often is associated with ‘Western lifestyle’ (24, 25), another interesting question is whether the socio-economic status (SES) influences disease expression. In contrast to other diseases, where morbidity and mortality decrease with higher SES (26–29), several studies have shown that the prevalence of AD increases with the SES of the family (19, 23, 30–33). Little is known about the mechanisms behind the association between SES and morbidity. In this article, we treat parental education as a surrogate measure for SES. An association between parental education and AD might arise if (i) higher parental education indicates a higher standard of living and ‘Western lifestyle’, (ii) better educated parents are more sensitive to AD symptoms in their children, (iii) better educated parents are more able to get referral and an AD diagnosis for their child and (iv) better educated parents are better able to remember AD episodes. In this article, we are able to present an independent association between the parents’ education and the prevalence of AD.

Methods

Two cross-sectional studies were conducted in Upper Austria (one of the nine Federal States of Austria, population approx. 1.4 million) along the ISAAC (International Study on Asthma and Allergy in Childhood) protocol. ISAAC was founded in 1991 to collect comparable results from studies about asthma, AD and allergic rhinitis and their influencing factors from as many countries as possible to identify differences in prevalence as well as possible risk factors. The different phases of the worldwide programme are described elsewhere (17, 34). In Upper Austria during ISAAC Phase I (1995–97), all elementary schools took part, whereas ISAAC Phase III (6 years later, 2001–03) had to be reduced to 7 of the 18 political districts because of time and cost restraints. To be able to compare the data, we reduced the data set of Phase I to the same seven districts: Eferding, Freistadt, Grieskirchen, Linz-Land, Perg, Urfahr-Umgebung and Wels-Land, representing a mixture of both rural and urban

areas. Unlike the original ISAAC protocol (17), we did not draw random samples of schools and school children but asked all parents of all children attending pre-school classes (5–6-year-olds) and first (6–7 years of age) and second grade classes (7–8 years of age) of all schools to participate in the survey. The parents were asked to fill in a standardized questionnaire about atopic diseases and their possible influencing factors. Data about AD in the child were collected by the following questions: (i) ‘Has your child ever had an itchy rash which was coming and going for at least 6 months?’, (ii) ‘Has your child had this itchy rash at any time in the last 12 months?’ and (iii) ‘Has your child ever had eczema (diagnosed by a doctor)?’ In the selected seven political districts in ISAAC Phase I, results from 13,399 questionnaires were obtained, and (6 years later) in ISAAC Phase III, 12,784 parents gave information about symptoms and individual risk factors.

Because of the fact that in some small schools, pupils are not spatially separated into several class rooms, and because we did not want to exclude older children from the survey, some children ($n = 4763$ in the first survey and $n = 4474$ in the second survey, respectively) older than 6–7 years of age were surveyed too. Moreover, in Austria some children start school not at the age of six, but their enrolment is delayed for a year. So to make sure that all 6-year-old children were included, we had to include pre-school classes as well. Thus, three children surveyed were 5 years old (all in ISAAC Phase III, none in Phase I).

Analyses were restricted to 6–9-year-old children. Answers to the questions about ever having itchy rash (= lifetime prevalence of AD), education of the parents and AD in the family were considered to be essential. Thus, all data sets of children with one or more information missing were excluded in both studies, ditto data sets of children without declared sex. Eventually, data from 12,115 (Phase I) and 11,468 (Phase III) children could be analysed, respectively.

To determine whether SES of the parents influences the appearance of AD in the child, odds ratios (OR) for the association between parental education and AD diagnosis and symptoms were calculated. Concerning parental education, two categories were defined: ‘low education’, which included parents finishing a compulsory or a professional school, and ‘high education’, meaning that parents had attended high school or university.

Several studies have detected that a positive history of AD in the parents is a strong risk

factor. So to avoid possible confounding, the OR were adjusted for the variable 'atopic dermatitis of the mother/father' (7, 14–20, 35).

All statistical analyses were performed using SPSS (version 13, SPSS Inc., Chicago, IL, USA) and Epi-Info (version 6.04d) computer packages. Besides descriptive statistics, OR and the corresponding 95% confidence intervals (95%CI) were calculated to report associations. 'High education' was compared with 'low education', which served as the reference group. To avoid potential confounding including maternal and paternal history of atopic dermatitis, adjusted OR according to Mantel and Haenszel (36) were calculated.

Results

Between 1995 and 1997 (ISAAC Phase I Study), a total of 37,717 questionnaires covering all children attending pre-school classes and first and second grade of all elementary schools in Upper Austria were distributed. Of them, 35,238 were returned representing a response rate of 93.4%. To guarantee comparability, in analysis this data set of ISAAC Phase I was reduced to the same seven districts covered in Phase III, which results in 13,399 questionnaires. After reducing data to 6–9-year-olds and excluding all data sets of children with missing information on sex, lifetime itchy rash, parental education and parental history of AD, 12,115 valid questionnaires (90.4%) remained for analyses.

During ISAAC Phase III, all 13,731 pupils attending pre-school classes and first and second grade of all elementary schools in seven political districts of Upper Austria (Eferding, Freistadt, Grieskirchen, Linz-Land, Perg, Urfahr-Umgebung and Wels-Land) received questionnaires, from which 12,784 were returned, resulting in a response rate of 93.1%. After selecting children aged 6–9 and with 'sex' and information on the above-mentioned variables given, 11,468 valid questionnaires remained for analysis (89.7%).

Detailed information about the study population including parental education and parental AD is presented in Table 1. Frequency distributions of parental education differed considerably between the two study periods (fathers and mothers, $p < 0.001$). After 6 years time, a trend to higher education (high school and university) is noticeable. Similar to their children, prevalence of AD rose in parents too ($p < 0.001$), albeit on a much lower level and by a lower magnitude.

In 6–9-year-old children, the prevalence of an AD diagnosis from a doctor is higher than the

Table 1. Demographic variables of the study populations in ISAAC Phases I and III (seven political districts of Upper Austria)

	ISAAC I (1995–97)		ISAAC III (2001–03)	
	n	%	n	%
Mean age years	7.19		7.18	
Sex				
Male	6282	51.9	5901	51.5
Female	5833	48.1	5567	48.5
AD				
AD ever	1158	9.6	1524	13.3
Rash ever	1114	9.2	1256	11.0
Rash 12	721	6.0	769	6.7
Parental AD				
Mother	446	3.7	541	4.7
Father	255	2.1	325	2.8
Maternal Education				
Compulsory school	3238	26.7	2298	20.0
Professional school	6089	50.3	5745	50.1
High school	2200	18.2	2667	23.3
University	588	4.9	758	6.6
Paternal Education				
Compulsory school	1239	10.7	946	8.2
Professional school	8096	66.8	7496	65.4
High school	1736	14.3	1950	17.0
University	990	8.2	1076	9.4

ISAAC, International Study on Asthma and Allergy in Childhood; AD ever, lifetime diagnosis (by a doctor) of AD; Rash ever, lifetime symptoms (itchy rash) of AD; Rash 12, itchy rash in the past 12 months.

lifetime prevalence of AD symptoms. Table 2 gives the prevalence of AD diagnoses and symptoms by the children's age.

The prevalence of AD and its symptoms in the children surveyed according to sex is given in Table 3. All variables examined demonstrate girls to be more affected.

Parental education, which we considered to be a proxy representation of the family's SES, mostly seems to influence the lifetime prevalence of AD diagnosis, whereas the variable 'AD symptoms in the last 12 months' is not associated with it (Table 4). It should be noted that the

Table 2. Absolute number (n) and percentage (%) of children with an AD diagnosis and with symptoms by age (seven political districts of Upper Austria)

	ISAAC I			ISAAC III		
	AD ever n (%)	Rash ever n (%)	Rash 12 n (%)	AD ever n (%)	Rash ever n (%)	Rash 12 n (%)
Age						
6	224 (9.4)	223 (9.3)	136 (5.7)	281 (12.2)	234 (10.1)	137 (5.9)
7	519 (9.5)	491 (9.0)	317 (5.8)	697 (13.8)	552 (10.8)	334 (6.5)
8	386 (10.3)	366 (9.7)	244 (6.5)	502 (13.8)	425 (11.6)	275 (7.5)
9	29 (6.4)	34 (7.4)	24 (5.2)	44 (11.8)	45 (13.5)	23 (6.1)
All	1158 (9.6)	1114 (9.2)	721 (6.0)	1524 (13.4)	1256 (11.0)	769 (6.7)

ISAAC, International Study on Asthma and Allergy in Childhood; AD ever, lifetime diagnosis (by a doctor) of AD; Rash ever, lifetime symptoms (itchy rash) of AD; Rash 12, itchy rash in the past 12 months.

educational level of the mother has a stronger effect on AD symptoms and diagnosis in the child than that of the father. Adjusting for parental AD did not result in a major change in OR for the comparison of high to low maternal and paternal education, respectively. Detailed information about the results of the calculations is given in Table 4. Independently of a possible AD disease of the parents, high parental education increases the risk for AD in the child by between 18% and 41%.

Whereas results concerning AD symptoms in the last 12 months remained almost stable from ISAAC Phase I to Phase III, parental education seemed to have a stronger influence on lifetime AD diagnosis in Phase I compared to Phase III. Concerning the variable 'AD symptoms ever', parental education had a stronger influence in Phase III compared to Phase I.

Discussion

From ISAAC Phase I (1995–97) to Phase III (2001–03), the prevalence of AD in Upper Austrian children increased in all variables examined. This result goes along with a multitude of other comparable studies: among others, four cross-sectional surveys conducted between 1992 and 2001 in Switzerland (5), a country which is very similar to Austria concerning the SES. Taking all four Swiss studies together, a total of 5446 children participated. The authors observed an increase over time also in AD symptoms during the last 12 months (1992: 4.6%, 1995: 6.5%, 1998: 7.4% and 2001: 7.6%) – notably more accentuated in girls than in boys. Galassi et al. (25) described a rise in prevalence in an Italian study ($n = 27,402$) between the years 1994 and 2002. Lee et al. (10) analysed 12–15-year-old adolescents ($n = 53,134$) in Taiwan likewise in 1995 and 2001 and also described an increasing prevalence of AD, where – comparable to our results – girls were more often affected than boys. In contrast to these outcomes, a

Table 4. Odds ratio (OR) for AD symptoms and diagnosis in the child depending on high parental education (low parental education OR = 1)

Parent	OR (95% CI)	OR _{mm} [†] (95% CI)
ISAAC I		
AD ever		
Mother	1.40 (1.22–1.61)*	1.37 (1.19–1.58)*
Father	1.41 (1.23–1.62)*	1.37 (1.19–1.58)*
Rash ever		
Mother	1.24 (1.08–1.43)*	1.22 (1.05–1.41)*
Father	1.15 (0.99–1.33)	1.13 (0.97–1.31)
Rash 12		
Mother	0.80 (0.60–1.06)	0.80 (0.60–1.07)
Father	0.78 (0.58–1.04)	0.76 (0.57–1.03)
ISAAC III		
AD ever		
Mother	1.26 (1.12–1.42) *	1.25 (1.11–1.41)*
Father	1.22 (1.08–1.37) *	1.18 (1.05–1.34)*
Rash ever		
Mother	1.31 (1.16–1.49) *	1.31 (1.15–1.48)*
Father	1.29 (1.13–1.47) *	1.24 (1.09–1.41)*
Rash 12		
Mother	0.82 (0.64–1.05)	0.82 (0.64–1.05)
Father	0.82 (0.63–1.05)	0.77 (0.60–1.00)

ISAAC, International Study on Asthma and Allergy in Childhood.

*Statistically significant ($p < 0.05$).

[†]OR adjusted (Mantel-Haenszel) for AD in parents.

decrease in prevalence was observed in some European countries, e.g. Great Britain, Ireland, Sweden and Germany, but also in New Zealand (37). Globally seen, the prevalence does not follow homogeneous trends. The predominance of AD in girls, which was observed in our study, as well as in the studies mentioned above, is an interesting fact to reflect on. A possible explanation could be a different view of mothers on their boys vs. girls skin condition, also influenced by considerations of cosmetics and beauty.

In our studies of Upper Austrian children, the question whether disease labelling by doctors influenced prevalence arises. Hence, it is unsure whether the same child seen by different doctors would receive the same diagnosis. Another influencing factor might be parents' intensified awareness towards health and subsequently their

Table 3. Absolute number (n) and percentage (%) of children with an AD diagnosis and with symptoms by sex

	ISAAC I			ISAAC III		
	AD ever n (%)	Rash ever n (%)	Rash 12 n (%)	AD ever n (%)	Rash ever n (%)	Rash 12 n (%)
Sex						
Male	553 (8.7)	517 (8.2)	313 (5.0)	759 (12.9)	600 (10.2)	346 (5.9)
Female	605 (10.4)	597 (10.2)	408 (7.0)	765 (13.9)	656 (11.8)	423 (7.6)
All	1158 (9.6)	1114 (9.2)	721 (6.0)	1524 (13.4)	1256 (11.0)	769 (6.7)

ISAAC, International Study on Asthma and Allergy in Childhood; AD ever, lifetime diagnosis (by a doctor) of AD; Rash ever, lifetime symptoms (itchy rash) of AD; Rash 12, itchy rash in the past 12 months.

earlier seeking for medical advice. Additionally, an increase in unspecific skin disorders could have happened, which are labelled 'atopic dermatitis' by the parents, but this is contrasted by the fact that also the lifetime prevalence of AD diagnosis by a doctor has increased. Furthermore, annual fluctuations in environment might be a strong factor in the expression of this disease.

Concerning parental education, we observed that the participating parents had higher school education in the second survey compared to the first survey: whereas in ISAAC Phase I, 23.1% of the mothers and 22.5% of the fathers were highly educated (i.e. graduation of a high school or university), in ISAAC Phase III percentages were 29.9% (+6.8%) and 26.4% (+3.9%), respectively. Parallel to this development, also the prevalence of AD symptoms and diagnosis increased as described previously. As the parental education level should be a good surrogate measure for the family's SES, the question arises whether there is an association between the rising wealth in families and the increase in AD prevalence in the age group examined. Du Prel et al. (38) examined pre-school children's health and its association with parental education in East and West Germany. The authors suggested that SES has a strong influence on people's health, which may particularly also be the case in the matter of atopic disease. They noticed that environmental risk factors may differ, depending on SES. Likewise, Lee et al. (10) found that the prevalence of atopic disease rises with the family's SES. They even stated that higher education of the parents is the strongest risk factor for AD in the child. Other findings suggest that lifetime prevalence rates of atopic diseases and symptoms are highest in children from highly educated parents (6, 7, 39). It has been postulated that the access to 'Western lifestyle' (associated with higher SES) may be responsible for the rising prevalence in allergic diseases (8, 24, 40–43). However, several biases could have influenced these findings: Lower SES implicates a poorer health education and knowledge and therefore a lower perception of being ill as Mercer et al. (8) have described in their study. Another possible bias is the restricted access of less educated parents to medical care (8, 38, 44). In Austria, a compulsory health insurance system is established. This should keep access thresholds for people low, compared to countries with mainly private insurance. Moreover, better parental education implicates (besides an easier access to the health care system) a sophisticated health education and therefore an earlier perception of

disease symptoms (39, 45). Maybe, better educated parents take their children to a doctor earlier (38, 39, 46) and report milder symptoms, too (44, 47–49). Recall of the children's diagnoses may also depend on parental education (39, 48, 49), but at the moment, a diagnosis of atopic dermatitis and the use of the term 'allergy' seem to be 'fashionable' and might have also contributed to the rise in prevalence (37, 38). Additionally, it could be considered that higher educated parents tend to be more worried about their children's health than less educated (7, 39). We hypothesize that the fact that AD is more closely related to maternal than paternal education (also found by Dom et al., 50) is caused by the fact that well-educated mothers are better able to interpret possible symptoms of AD, and it is mothers who more likely have filled in the questionnaire.

Another important question regarding the association between higher SES and increasing prevalence of AD arises: Are better educated parents cleaner? According to the hygiene hypothesis, fewer germs exist because of cleanliness and children acquire fewer infections. Furthermore, it is hypothesized that this way the immune system does not get trained enough because of the missing accurate challenge. Therefore, the risk for acquiring an atopic disease should increase. A cross-sectional survey in rural areas of Austria, Germany and Switzerland examines this hypothesis: according to the authors, long-term and early-life contact with stables and farm-milk induces a strong protective effect against the development of atopic diseases (51). Other studies contribute to these findings too: Holgate (52) found higher AD prevalence rates because of missing stimulation of the immune system during critical periods of development. Strachan et al. (53) detected a protective effect of early infections on allergic diseases. Du Prel et al. (38) consider factors related to hygiene, for example (i) being a single child and therefore getting fewer infections or (ii) unfavourable indoor air, as strong determinants of allergic diseases. Moreover, according to Harris et al. (18) interventions to reduce house dust mite in early infancy could increase the risk for AD. Because we did not collect data about the children's housing, we are not able to correct for this important influencing factor.

The mental component towards AD also deserves further research. By the assumption that higher educated parents earn more money, a protective effect on the probability of the child becoming ill can be expected. It appears that in wealthier families, parents have to worry less

about maintaining the household, and therefore the 'inner family stress level' should be lower than in families in economically weaker positions. Because the contrary is the case, possibly a neglect of the children by their employed parents could be a reason for the increased prevalence rate of AD in financially secured children. Several studies suggest that stress increases the risk of AD. Bockelbrink et al. (54) concluded that divorce or separation of the parents, which means a heavy mental burden for the child, is associated with a significant increase in incidence of AD. Another important influencing factor might be that better educated parents are more demanding towards their children. This behaviour exerts much pressure on the children.

Up until now, no single environmental or genetic risk factor was able to explain the worldwide changes in prevalence of AD. Apparently, risk factors alter differently by time in different countries of the world (37). The access to the Western lifestyle and the associated pursuit of higher SES seem to influence the disease too, which is supported by our study on a large sample of children. However, one should bear in mind that results of self-reporting questionnaire studies are subject to cultural, educational, psychological and language factors (1, 55). In the future, an interesting analysis will be which parental education, the maternal or the paternal one, has a stronger effect on AD in the child. We plan to pursue this question, on an even larger sample of children.

The fact that the very high participation rate (higher than 90%, nearly resembling a census) emphasises our findings is attenuated by the healthy worker effect. It is possible that ill children (children with atopic disease) did not attend school at the time of the survey because of their illness, and they may have missed the survey. To counteract this factor, the time given for completing the survey in the single school classes was extended to more than a week. Schools had also the possibility to send latecomers, and these were included into data entry.

In conclusion, parental education could be established as an independent risk factor for (diagnosis of) AD in children if our findings are confirmed in other studies which have to explicitly ask for the person who filled in the questionnaire and if the recall capacity of the parents is investigated and can be treated separately in analyses.

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References

1. WILLIAMS H, ROBERTSON C, STEWART A, et al. World-wide variations in the prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. *J Allergy Clin Immunol* 1999; 103: 125–38.
2. SPERGEL JM, PALLER AS. Atopic dermatitis and the atopic March. *J Allergy Clin Immunol* 2003; 112 (Suppl. 6): 118–27.
3. SUGIURA H, UMEMOTO N, DEGUCHI H, et al. Prevalence of childhood and adolescent atopic dermatitis in a Japanese population: comparison with the disease frequency examined 20 years ago. *Acta Derm Venereol* 1998; 78: 293–4.
4. WILLIAMS HC. Is the prevalence of atopic dermatitis increasing? *Clin Exp Dermatol* 1992; 17: 385–91.
5. GRIZE L, GASSNER M, WÜTHRICH B, et al. Trends in prevalence of asthma, allergic rhinitis and atopic dermatitis in 5–7-year old Swiss children from 1992 to 2001. *Allergy* 2006; 61: 556–62.
6. SCHÄFER T, KRÄMER U, VIELUF D, ABECK D, BEHRENDT H, RING J. The excess of atopic eczema in East Germany is related to the intrinsic type. *Br J Dermatol* 2000; 143: 992–8.
7. ZUTAVERN A, HIRSCH T, LEUPOLD W, WEILAND S, KEIL U, VON MUTIUS E. Atopic dermatitis, extrinsic atopic dermatitis and the hygiene hypothesis: results from a cross-sectional study. *Clin Exp Allergy* 2005; 35: 1301–8.
8. MERCER MJ, JOUBERT G, EHRLICH RI, et al. Socioeconomic status and prevalence of allergic rhinitis and atopic eczema symptoms in young adolescents. *Pediatr Allergy Immunol* 2004; 15: 234–41.
9. VERBOOM P, HOKKAART-VAN L, STURKENBOOM M, DE ZEEUW R, MENKE H, RUTTEN F. Epidemiology and health services research. The cost of atopic dermatitis in the Netherlands: an international comparison. *Br J Dermatol* 2002; 147: 716–24.
10. LEE YL, LI CW, SUNG FC, GUO YL. Increasing prevalence of atopic eczema in Taiwanese adolescents from 1995 to 2001. *Clin Exp Allergy* 2007; 37: 543–51.
11. SANDSTROM MH, FAERGEMANN J. Prognosis and prognostic factors in adult patients with atopic dermatitis: a long-term follow-up questionnaire study. *Br J Dermatol* 2004; 150: 103–10.
12. THE INTERNATIONAL STUDY OF ASTHMA AND ALLERGIES IN CHILDHOOD (ISAAC) STEERING COMMITTEE. World-wide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 1998; 351: 1225–32.
13. ASHER MI, MONTEFORT S, BJÖRKSTÉN B, et al. World-wide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multi-country cross-sectional surveys. *Lancet* 2006; 368: 733–43. Erratum in: *Lancet* 2007 Sep 29; 370(9593): 1128.
14. BOHME M, SVENSSON A, KULL I, NORDVALL SL, WAHLGREN CF. Clinical features of atopic dermatitis at two years of age: a prospective population based case-control study. *Acta Derm Venereol* 2001; 81: 193–7.
15. BLEIKER TO, SHAHIDULLAH H, DUTTON E, GRAHAM-BROWN RA. The prevalence and incidence of atopic dermatitis in a birth cohort: the importance of a

- family history of atopy. *Arch Dermatol* 2000; 136: 274–5.
16. MATSUOKA S, NAKAGAWA R, NAKAYAMA H, YAMASHITA K, KURODA Y. Prevalence of specific allergic diseases in school children as related to paternal atopy. *Pediatr Int* 1999; 41: 46–51.
17. ASHER MI, KEIL U, ANDERSON HR, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995; 8: 483–91.
18. HARRIS JM, WILLIAMS HC, WHITE C, et al. Early allergen exposure and atopic eczema. *Br J Dermatol* 2007; 156: 698–704.
19. TAYLOR B, WADSWORTH J, GOLDING J, BUTLER N. Breast feeding, eczema, asthma, and hay fever. *J Epidemiol Community Health* 1983; 37: 95–9.
20. HARRIS JM, CULLINAN P, WILLIAMS HC, et al. Environmental associations with eczema in early life. *Br J Dermatol* 2001; 144: 795–802.
21. ARRUDA LK, SOLE D, BAENA-CAGNANI CE, NASPITZ CK. Risk factors for asthma and atopy. *Curr Opin Allergy Clin Immunol* 2005; 5: 153–9.
22. COLEMAN R, TREMBATH RC, HARPER JI. Genetic studies of atopy and atopic dermatitis. *Br J Dermatol* 1997; 136: 1–5.
23. AL-SAEED WY, AL-DAWOOD KM, BUKHARI IA, BAHNASSY AA. Risk factors and co-morbidity of skin disorders among female schoolchildren in Eastern Saudi Arabia. *Invest Clin* 2007; 48: 199–212.
24. WICHMANN H-E. Possible explanation for the different trends of asthma and allergy in East and West Germany. *Clin Exp Allergy* 1996; 26: 621–3.
25. GALASSI C, DE SARIO M, BIGGERI A, et al. Changes in prevalence of asthma and allergies among children and adolescents in Italy: 1994–2002. *Pediatrics* 2006; 117: 34–42.
26. MARMOT MG, SMITH GD, STANSFELD S, et al. Health inequalities among British civil servants: the Whitehall II study. *Lancet* 1991; 337: 1387–93.
27. MARMOT MG, SHIPLEY MJ, ROSE G. Inequalities in death-specific explanations of a general pattern? *Lancet* 1984; 1: 1003–6.
28. WORLD HEALTH ORGANIZATION. The World Health Report 2000 Health Systems: Improving Performance. Geneva: WHO 2000: 164–76.
29. HELMERT U, SHEA S. Social inequalities and health status in western Germany. *Public Health* 1994; 108: 341–56.
30. WILLIAMS HC, STRACHAN DP, HAY RJ. Childhood eczema: disease of the advantaged? *BMJ* 1994; 308: 1132–5.
31. LEWIS SA, BRITTON JR. Consistent effects of high socioeconomic status and low birth order, and the modifying effect of maternal smoking on the risk of allergic disease during childhood. *Respir Med* 1998; 92: 1237–44.
32. PETERS TJ, GOLDING J. The epidemiology of childhood eczema: II. Statistical analyses to identify independent early predictors. *Paediatr Perinat Epidemiol* 1987; 1: 80–94.
33. APFELBACHER CJ, OLLERT M, RING J, BEHRENDT H, KRÄMER U. Contact to cat or dog, allergies and parental education. *Pediatr Allergy Immunol* 2010; 21: 284–91.
34. ELLWOOD P, ASHER MI, BEASLEY R, CLAYTON TO, STEWART AW, ISAAC STEERING COMMITTEE. The international study of asthma and allergies in childhood (ISAAC): phase three rationale and methods. *Int J Tuberc Lung Dis* 2005; 9: 10–6.
35. KLÜKEN H, WIENKER T, BIEBER T. Atopic eczema/dermatitis syndrome – a genetically complex disease. New advances in discovering the genetic contribution. *Allergy* 2003; 58: 5–12.
36. BRESLOW NE, DAY NE. Statistical Methods in Cancer Research Volume 1 – The Analysis of Case-Control Studies. IARC Scientific Publications 32. Lyon: World Health Organization and International Agency for Research on Cancer, 1980.
37. WILLIAMS H, STEWART A, VON MUTIUS E, COOKSON W, ANDERSON HR, INTERNATIONAL STUDY OF ASTHMA AND ALLERGIES IN CHILDHOOD (ISAAC) PHASE ONE, THREE STUDY GROUPS. Is eczema really on the increase worldwide? *J Allergy Clin Immunol* 2008; 121: 947–54.
38. DU PREL X, KRÄMER U, BEHRENDT H, et al. Pre-school children's health and its association with parental education and individual living conditions in East and West Germany. *BMC Public Health* 2006; 6: 312.
39. HEINRICH J, POPESCU MA, WJST M, GOLDSTEIN IF, WICHMANN HE. Atopy in children and parental social class. *Am J Public Health* 1998; 88: 1319–24.
40. WILLIAMS H. Atopic eczema. We should look on the environment. *Br Med J* 1995; 311: 1241–2.
41. WAITE DA, EYLES EF, TONKIN SL, O'DONNELL TV. Asthma prevalence in Tokelauan children in two environments. *Clin Allergy* 1980; 10: 71–5.
42. WILLIAMS HC, PEMBROKE AC, FORSDYKE H, BOODOO G, HAY RJ, BURNEY PGJ. London-born black Caribbean children are at increased risk of atopic dermatitis. *J Am Acad Dermatol* 1995; 32: 212–7.
43. RING J, KRÄMER U, SCHÄFER T, ABECK D, VIELUF D, BEHRENDT H. Environmental risk factors for respiratory and skin atopy: results from epidemiological studies in former East and West Germany. *Int Arch Allergy Immunol* 1999; 118: 403–7.
44. GEHRING U, PATTENDEN S, SLACHTOVA H, et al. Parental education and children's respiratory and allergic symptoms in the Pollution and the Young (PATY) study. *Eur Respir J* 2006; 27: 95–107.
45. SIBBALD B, RINK E. The labelling of rhinitis and hay fever by doctors. *Thorax* 1991; 46: 378–81.
46. WATERS WE. Migraine, social class, and familial prevalence. *BMJ* 1971; ii: 77–81.
47. NG MAN KWONG G, PROCTOR A, BILLINGS C, et al. Increasing prevalence of asthma diagnosis and symptoms in children is confined to mild symptoms. *Thorax* 2001; 56: 312–4.
48. WUTHRICH B. Epidemiology of the allergic diseases: are they really on the increase? *Int Arch Allergy Appl Immunol* 1989; 90: 3–10.
49. TAYLOR B, WADSWORTH J, WADSWORTH M, PECKHAM C. Changes in the reported prevalence of childhood eczema since the 1938–45 war. *Lancet* 1984; ii: 1255–7.
50. DOM S, DROSTE JH, SARIACHVILI MA, et al. The influence of parental educational level on the development of atopic sensitization, wheezing and eczema during the first year of life. *Pediatr Allergy Immunol* 2009; 20: 438–47.
51. RIEDLER J, BRAUN-FAHRLÄNDER C, EDER W, et al. Exposure to farming in early life and development of

- asthma and allergy: a cross-sectional survey. *Lancet* 2001; 358: 1129–33.
52. HOLGATE ST. The epidemic of allergy and asthma. *Nature* 1999; 402: B2–4.
53. STRACHAN DP, HARKINS LS, JOHNSTON ID, ANDERSON HR. Childhood antecedents of allergic sensitization in young British adults. *J Allergy Clin Immunol* 1997; 99: 6–12.
54. BOCKELBRINK A, HEINRICH J, SCHÄFER I, et al. Atopic eczema in children: another harmful sequel of divorce. *Allergy* 2006; 61: 1397–402.
55. STRACHAN D, SIBBALD B, WEILAND S, et al. Worldwide variations in prevalence of symptoms of allergic rhinoconjunctivitis in children: the International Study of Asthma and Allergies in Childhood (ISAAC). *Pediatr Allergy Immunol* 1997; 8: 161–76.