

The Prevalence of Allergic Sensitisation in Immigrant Children in the Netherlands

J.G.C. van Amsterdam^a E.W.M.A. Bischoff^a M. Hady^b A. Opperhuizen^a
P.A. Steerenberg^a

^aLaboratory for Toxicology, Pathology and Genetics, National Institute for Public Health and the Environment, Bilthoven, ^bMunicipal Health Service, Utrecht, The Netherlands

Key Words

Prevalence, allergy · Allergic sensitisation · Immigrants, the Netherlands · Skin prick test · Exhaled nitric oxide

Abstract

Background: Differences in the prevalence of allergic sensitisation have been reported in immigrant children living in the same urban environment. The purpose of this study is to investigate the prevalence of allergic sensitisation in school children of Dutch, Turkish and Moroccan origin. **Methods:** The prevalence of sensitisation to aero-allergens was assessed using the skin prick test in a non-selected sample of 512 children (response rate 54%) living in the same inner city district of Utrecht. In addition, exhaled nitric oxide (Fe_{NO}) was determined. **Results:** The prevalence of allergic sensitisation was dependent on the ethnic origin. As compared with Dutch children (19.1%), a higher prevalence of allergic sensitisation was observed in immigrant children for whom both parents were born in Turkey (23.6%, not significant) or Morocco (30.6%, $p < 0.05$). The prevalence of allergic sensitisation in Dutch children was nearly 2 times lower than the reported prevalence in German children. In all sensitised children, the mean Fe_{NO} value was significant-

ly ($p < 0.05$) higher than in non-sensitised children, and the mean Fe_{NO} level was highest in Moroccan children sensitised to indoor allergens. **Conclusion:** In the Netherlands, immigrant children show a higher prevalence of allergic sensitisation as compared to Dutch children.

Copyright © 2004 S. Karger AG, Basel

Introduction

For some decades, the prevalence of allergy and asthma has been increasing. Allergic diseases are common, affecting between 15 and 30% of all children in Western countries. The European Community Respiratory Health Survey has shown a wide geographical variation in the reported prevalence of symptoms highly suggestive of asthma, current hay fever or nasal allergies in adults. Similar observations have been made in children in the framework of the International Study of Asthma and Allergies in Childhood [1]. In general, symptoms are more common in New Zealand, Australia, the British Isles and the United States than in mainland Europe, although there is wide variation even within some countries [2].

Many factors assumed to be responsible for this increase have been mentioned in relation with personal

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

© 2004 S. Karger AG, Basel
1018–2438/04/1333–0248\$21.00/0

Accessible online at:
www.karger.com/iaa

Correspondence to: Dr. J.G.C. van Amsterdam
RIVM, PO Box 1
NL–3720 BA Bilthoven (The Netherlands)
Tel. +31 30 274 2888, Fax +31 30 274 4446
E-Mail JGC.van.Amsterdam@rivm.nl

hygiene, food consumption and air pollution [3]. Family history of allergy is the most prominent risk factor for allergic disease [4–7], but other socio-demographic factors, like economic status, number of siblings and birth order [8], show strong associations as well.

Studies performed in countries characterised by differences in the prevalence of allergic disease, lifestyle and environment, e.g. studies comparing West versus East Germany [9, 10], and Poland versus Estonia and Sweden [11], have not revealed well-defined causal relationships.

In the past, immigrant studies have shown the importance of lifestyle in relation to breast cancer [12]. Similarly, two recent German studies have assessed the prevalence of allergy in immigrants and their native peers. These studies showed that the prevalence of allergy was lower in children with parents from Mediterranean countries as compared with children of native parents [13, 14]. In contrast, Dutch immigrant children more often have respiratory symptoms in the first years of life than Dutch children [15], and children from Chilean immigrants in Sweden had a higher prevalence of allergic asthma and allergic rhinitis than children from Swedish parents [16]. This Swedish interview-based study, however, also showed a relatively low prevalence of allergic disease in Turkish children as compared with Chileans. In the present study, the prevalence of allergic sensitisation in a non-selected sample of Dutch and immigrant school children was assessed to investigate whether ethnic subgroups in the Netherlands show differences in the prevalence of allergic sensitisation. Finally, we recently showed that exhaled nitric oxide (FeNO) is associated with respiratory symptoms diagnosed by a doctor in symptomatic as compared to non-symptomatic children [17]. FeNO , which may therefore be regarded as a surrogate marker of allergic sensitisation, was measured to support the findings.

Materials and Methods

Study Population

The study was performed in a non-selected sample of children (7–14 years, mean age 10.1 years) born in the Netherlands and attending primary schools in an inner city district ('Zuilen-Ondiep') of the town Utrecht in the Netherlands. The parents of 889 children (76%) responded to the invitation sent out via the school, and 637 of the responding parents (72%) gave their child permission to participate in the study. Children below the age of 7 years were excluded because they could not exhale air in a reproducible way. No other specific exclusion criteria were applied. A total of 512 children were finally evaluated in this study.

Ethnicity of the child was defined according to the ethnicity of both parents, i.e. the country of origin of the parents: the Nether-

lands, Turkey, Morocco, Surinam (i.e. Dutch Guyana) or 'other'. Forty-nine children born from parents with another ethnic background or from mixed couples (parents who differed in ethnic origin) were categorised as 'other'. According to the postal code of the home address, all children lived in the same inner city district within 1 mile from their primary school. This study location was chosen because of the presumed low variation in indoor and outdoor quality of housing conditions (no high-rise blocks, and similarity in exterior green facilities, traffic intensity and distance from motorways). The study protocol was approved by the Medical Ethics Committee of the National Institute for Public Health and the Environment-Netherlands Organisation for Applied Scientific Research.

Assessment of Allergic Sensitisation

Allergic sensitisation status was assessed by the skin prick test. The five aero-allergens tested were dog dander, cat dander, *Dermatophagoides pteronyssinus* (house dust mite; HDM), mixed tree pollen (*Betula verrucosa*, *Alnus glutinosa*, *Corylus avellana*) and mixed grass pollen (*Dactylis glomerata*, *Lolium perenne*, *Festuca pratensis*, *Poa pratensis*, *Phleum pratense*, *Avena eliator*). Standardised allergen extracts and positive and negative controls (saline and histamine 10 mg/ml) were provided by ALK (Copenhagen, Denmark). The test was performed on the volar side of the left forearm using ALK lancets. After 15 min, the outside contour of the wheal was measured, and the mean of the longest diameter and the length of the perpendicular line through its middle was calculated. Allergic sensitisation to indoor allergens was defined as a positive cutaneous reaction to at least HDM (none of the children was only sensitive to animal dander), while allergic sensitisation to outdoor allergens was defined as a positive cutaneous reaction to grass or tree pollen. According to the instructions of the supplier (ALK-Abello), a wheal size larger than 2 mm and a ratio of wheal to allergen and positive control >0.4 are considered a positive allergic reaction. Testing by the criterion 'wheal size >2 mm after subtraction of the negative control' did not affect the results.

Measurement of FeNO

Exhaled air of the children was sampled in balloons using a sampling device equipped with a 'pre-balloon' of 500 ml to exclude dead space volume from the sample, as previously described [18]. In short, children exhaled air at 10–20 cm of water back pressure into NO-impermeable aluminium foil bags of 500 ml (Mylar balloon, ABC Ballonnen, Zeist, The Netherlands). After exhalation into the 'pre-balloon' at a high speed of 6,000 ml/min, exhaled air was collected at a low flow rate of 500 ml/min to obtain relatively high FeNO concentrations. The 1,000 ml of air containing ambient NO or NO from the dead space was collected in the pre-balloon and discarded. Although this method differs from those recommended by the European Respiratory Society and American Thoracic Society [19, 20], we have shown previously that it correlates well with on-line measurements made in the laboratory following European Respiratory Society and American Thoracic Society recommendations [21].

Outdoor air was sampled in aluminium foil air bags by an air sampling pump (model P-200, Dupont de Nemours & Company Inc., Wilmington, Del., USA) to control for exceptionally high ambient NO levels, known to affect the measurement of FeNO [22]. If the ambient NO level was >50 ppb, the air sampling and measurement of FeNO was interrupted and continued on another day. Ambient temperature was measured continuously. A rapid-response chemiluminescence analyser (Sievers 280B, Boulder, USA) with a response time <200 ms was used to determine the concentration of

Table 1. Characteristics and prevalence (percentage in parentheses) of allergic sensitisation to aeroallergens in the total sample (n = 512) and the allergic sensitivity in a sub-sample of school children (n = 463; 7–14 years, mean age 10.1 years)

Variable	Boys	Girls	All	Mean age years
<i>Subjects</i>				
Dutch parents	122 (50.6)	119 (49.4)	241	10.1
Turkish parents	41 (60.3)	27 (39.7)	68	10.2
Moroccan parents	62 (46.3)	72 (53.7)	134	10.0
Surinam parents	14 (70.0)	6 (30.0)	20	10.2
Others ¹	20 (40.8)	29 (59.2)	49	10.1
<i>Skin prick positivity</i>				
Overall (n = 512)	72 (27.8)	63 (24.9)	135 (26.4)	
Overall (n = 463)	64 (26.8)	51 (22.8)	115 (24.8)	
To indoor allergens ²	45 (18.8)	42 (17.6)	87 (18.8)	
To outdoor allergens ³	30 (12.6)	29 (12.1)	59 (12.7)	
To indoor and outdoor allergens	11 (4.6)	20 (8.4)	31 (6.7)	

¹ Parents differing with respect to ethnic origin.
² Sensitive to at least HDM (and occasionally also to dog or cat dander, in addition to HDM).
³ Sensitive to grass or tree pollen.

Fe_{NO}. The analyser sample flow rate was kept constant at 200 ml/min. Fe_{NO} concentration was measured within 4 h after sampling. In the aluminium foil bags, the NO concentration remains constant for at least 48 h.

Measurement of Der p 1

Dust samples were collected from the child's mattress surface with a vacuum cleaner fitted with paper filters (Schleicher and Schuell 589, Dassel, Germany) for 2 min, regardless of the surface area of the mattress [23]. Paper filters were put in plastic petri dishes and weighed before sampling after at least 24 h of equilibration at 20°C and 50% relative humidity. Collected dust was frozen at –20°C until analysis. Total dust was assayed by weighing, and dust extracts were analysed using sandwich EIA (Indoor Biotechnologies, Cardiff, UK) with mouse IgG anti-mite monoclonal antibody 5H8 as catching antibody for Der p 1.

Questionnaire

A short questionnaire with questions about the ethnic background and allergic sensitisation status of the child (confirmed or not by a physician) and parents was filled in by the parents of the participating children. The questionnaire included the following questions on allergic health complaints and related issues which had to be answered by yes or no: Is your child allergic (has hay fever)? Was this confirmed by a physician? Indicate the type of allergy (from a panel of 10 items). Does your child have asthma? Was this confirmed by a physician? Does your child often sneeze? Does your child often have itching eyes? Does your child often have a running nose? Do the former complaints occur in the months May/June? Does your child often have a cold? Does your child wheeze (for instance at exhalation)? Does your child cough at night (in bed)? Is one of the parents allergic or asthmatic? Do you have pets at home? If so, what sort of animal?

Considering the parents' relatively low educational level and poor mastery of the Dutch language, it was not considered feasible to ask additional health-related questions.

Statistics

The statistical significance of differences in Fe_{NO} levels was assessed by one-way ANOVA. A p value < 0.05 was considered significant.

Results

Table 1 summarises data on the characteristics and the prevalence of allergic sensitisation in the study population. Of the 512 children tested by skin prick, 135 children (26.4%) showed a positive cutaneous reaction to at least one of the five allergens. In the sub-sample of 463 children born from parents with the same ethnic background (Dutch, Turkish, Moroccan or Surinam), 87 children (18.8%) were sensitive to indoor allergens (HDM, occasionally also dog or cat dander), whereas 59 children (12.7%) were sensitive to outdoor allergens and 6.7% to both indoor and outdoor allergens. Table 1 further shows that the ethnic sub-samples were comparable with respect to gender and age.

Figure 1 (a small group of 20 Surinam children was omitted) shows considerable differences in the prevalence of allergic sensitisation among the ethnic groups studied. Children of parents with a Mediterranean ethnic back-

Fig. 1. Prevalence of sensitisation to airborne allergens in Dutch (n = 241), Turkish (n = 68) and Moroccan (n = 134) children as assessed by the skin prick test. Co-ordinate values denote sensitisation rates within the ethnic group. * p < 0.05 as compared with their Dutch peers.

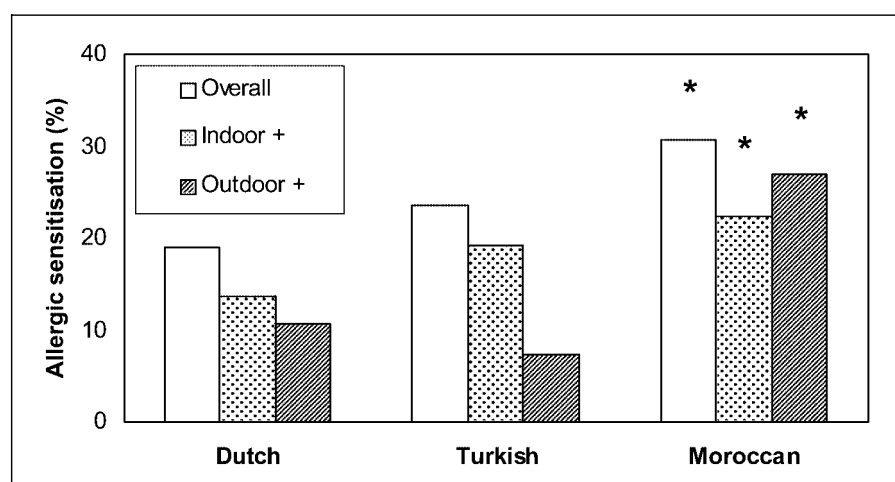


Table 2. Profile of allergic sensitisation in ethnic sub-groups taken from the total sample of 512 children

Variable	Origin of both parents				
	Dutch	Turkish	Moroccan	Surinam	other ¹
Total number	241	68	134	20	49
Skin prick test positive, %	19.1	23.6	30.6	60	37
One positive reaction, %	10.4	16.2	16.4	25	14.3
Two positive reactions, %	5.0	7.4	9.0	20	10.2
More than 2 positive reactions, %	3.7	0	5.2	15	12.2
History of allergy in one parent, %	31.3	31.4	29.7	40.0	28.6

¹ Parents differing with respect to ethnic origin.

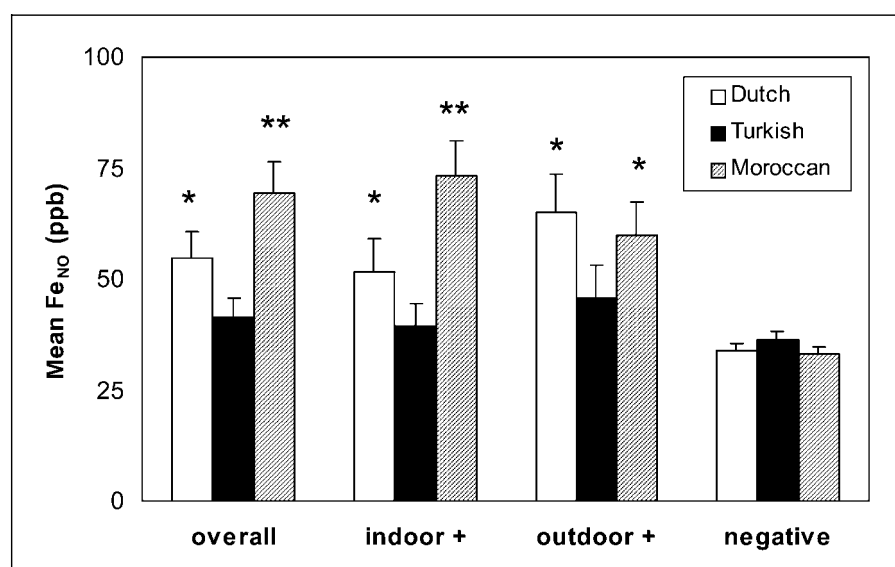
ground (Turkey and Morocco) showed a higher prevalence of overall allergic sensitisation as compared with their Dutch peers (23.6, 30.6 and 19.1%, respectively; $p < 0.05$ for Dutch versus Moroccan children). In addition, Moroccan children showed a high prevalence of allergic sensitisation to outdoor allergens (26.9%) as compared with Turkish (7.4%, not significant) and Dutch children (10.8%, $p < 0.05$). Children from parents who both had Surinam ethnic origin showed a high overall prevalence of allergic sensitisation of 50%, notably due to hypersensitivity to outdoor allergens (47%). The sensitisation rate to indoor allergens was lower in Dutch children (13.7%) as compared with Turkish (19.1%, not significant) and Moroccan children (22.4%, $p < 0.05$). Re-evaluation of the skin prick test using a cut-off value of 3 mm (instead of 2 mm) caused a drop from 23.3 to 16.9% in the overall sensitisation rate in the sample comprising Dutch, Turkish and Moroccan children. However, the differences in

the overall sensitisation rate between Dutch, Turkish and Moroccan children persisted, i.e. overall sensitisation rate of 13.3, 16.2 and 23.9%, respectively.

Skin prick testing was not performed in the parents [4–7], but evaluation of the health questionnaires revealed no difference in the reported prevalence of allergy between immigrant and Dutch parents (table 2), though the prevalence of allergy in Surinam parents was relatively high (40%). Table 2 further shows that multiple positive skin prick reactions (two or more) were more prevalent in Moroccan and Surinam children (14.2 and 35.0%, respectively), as compared with Dutch and Turkish children (8.7 and 7.4%, respectively).

It has been shown before that children who are sensitised to allergens have an increased Fe_{NO} value. The data depicted in figure 2 confirm this finding in the Dutch and Moroccan children, but surprisingly not in the Turkish sub-population, in whom the mean Fe_{NO} value was not

Fig. 2. Mean Fe_{NO} value in ethnic subgroups of children. * $p < 0.05$ as compared with non-sensitised peers. ** $p < 0.05$ as compared with their Dutch and Turkish peers.



significantly higher than the Fe_{NO} value of their non-sensitised counterparts. In addition, indoor allergen-sensitive Moroccan children showed a significantly higher mean Fe_{NO} level as compared with their Dutch peers.

Discussion

The present study shows an overall allergic sensitisation rate of 26.4% in a sample of 512 children living in an urban environment. This is slightly lower than the prevalence of 29.5% previously observed in a convenience sample of 450 children out of a total sample of 2,504 children using the standard International Study of Asthma and Allergies in Childhood phase II protocol [24]. In addition, the overall prevalence of allergic sensitisation in children from Turkish (23.6%) and Moroccan (30.6%) parents appeared to be higher ($p < 0.05$ for Moroccan children) than in children from Dutch parents (19.1%).

Following the hygiene hypothesis, there are a number of factors that may explain the observed differences in sensitisation rate. From the data available from the questionnaire, it seems, however, unlikely that the observed difference in sensitisation rate is due to the genetic background inherited from the parents [4–7]. No apparent difference was seen in the reported prevalence of allergy in the parents (except for the Surinam parents). Indoor air quality may also be involved in eliciting allergic sensitisation. Therefore, the levels of Der p 1 (*D. pteronyssinus* allergen) on the child's mattress and the floor of the living

room were measured in a random sample of the houses of 60 HDM-sensitive Dutch and immigrant children. It appeared that the mean Der p1 levels (HDM levels) of the sleeping mattress of Moroccan children were more than 3 times higher than those of Dutch or Turkish children (9,780 ng Der p1/g dust versus 2,960 and 2,590 ng/g dust, respectively). This higher exposure of Moroccan children to HDM could be responsible for the significantly higher mean Fe_{NO} level observed in the indoor allergen-sensitive Moroccan children as compared with their Dutch and Turkish peers.

In agreement with previous studies [24–26], the mean Fe_{NO} level of the sensitised children was positively associated with the number of allergens to which they were sensitised (results not shown). Table 2 shows that relatively more (nearly two-fold) Moroccan children were sensitised to more than one allergen than Dutch and Turkish children, whereas none of the Turkish children was sensitised to more than two allergens. This may explain the relatively high mean Fe_{NO} level observed in indoor allergen-sensitive Moroccan children.

We cannot account for a number of other factors which have been suggested to be involved in promoting the rate of allergic sensitisation. Due to the low education level and poor mastery of the Dutch language of the participating children's parents, it was not feasible to hand out long questionnaires to the parents of these children that include items like the respiratory health of parents and child, holding pets, number of siblings, type of floor covering and nutritional pattern. Indeed, differences in nutri-

tion patterns offer an attractive explanation. For example, the Dutch and Mediterranean kitchen differs with respect to the use of olive oil, i.e. unsaturated fatty acids, consumption of vegetables and type and quality of consumed meat (lean versus fat, saturated fats). Finally, the number of older siblings is unlikely to have served as a protective factor [8], because Moroccan mothers have 2- to 3-fold higher fertility rates than Dutch mothers [27].

Two recent German studies in school and pre-school children [13, 14] showed the reverse, i.e. a lower overall prevalence of allergic sensitisation in children with Turkish nationality living in Germany as compared with their German peers. The relatively low prevalence of allergic disease in Turkish children was confirmed in a Swedish interview study [16]. However, the various sensitisation rates of German children, as reported by Kabesch et al. [14], were considerably higher than those in their Dutch peers (e.g. overall sensitisation of 36.7 vs. 19.1%; pollen 31.0 vs. 11.6%; pets 24.7 vs. 7.5%; no difference with respect to HDM). In contrast, the various sensitisation rates of Turkish children from the present study were

comparable to those observed in the German study [14]. This difference between German and Dutch children is remarkably large, and cannot be solely due to the small methodological differences with respect to the skin prick test procedure (test panel of five versus six allergens, criterion of positive wheal) as applied by us and Kabesch et al. [14]. In addition, in agreement with the present results, it has been found that 'non-Dutch' toddlers (i.e. mothers born in non-Western countries) more often have respiratory symptoms in the first 2 years of life than Dutch children [15].

Considering the similarity of the two neighbouring nations with respect to race, climate, environment and dietary pattern, the large difference in the allergic sensitisation rate between Dutch and German children is intriguing, and urges further research.

It is concluded that the offspring of Moroccan immigrants in the Netherlands may have a higher risk of developing allergic asthma and atopic disease than Dutch children.

References

- Pearce N, Sunyer J, Cheng S, Chinn S, Björkstén B, Burr M, Keil U, Anderson HR, Burney P: Comparison of asthma prevalence in the ISAAC and the ECRHS. ISAAC Steering Committee and the European Community Respiratory Health Survey. International Study of Asthma and Allergies in Childhood. *Eur Respir J* 2000;16:420–426.
- Jarvis D, Burney P: ABC of allergies. The epidemiology of allergic disease. *BMJ* 1998;316:607–610.
- Steenberg PA, van Amsterdam JG, Vandebriel RJ, Vos JG, van Bree L, van Loveren H: Environmental and lifestyle factors may act in concert to increase the prevalence of respiratory allergy including asthma. *Clin Exp Allergy* 1999;29:1303–1308.
- Wright AL, Holberg CJ, Martinez FD, Halonen M, Morgan W, Taussig LM: Epidemiology of physician-diagnosed allergic rhinitis in childhood. *Pediatrics* 1994;94:895–901.
- Sibbald B, Rink E: Epidemiology of seasonal and perennial rhinitis: Clinical presentation and medical history. *Thorax* 1991;46:895–901.
- Kuehr J, Karmaus W, Forster J, Frischer T, Hendel-Kramer A, Moseler M, Stephan V, Urbanek R, Weiss K: Sensitization to four common inhalant allergens within 302 nuclear families. *Clin Exp Allergy* 1993;23:600–605.
- Wijga A, Smit HA, Brunekreef B, Gerritsen J, Kerkhof M, Koopman LP, Neijens HJ: Are children at high familial risk of developing allergy born into a low risk environment? The PIAMA Birth Cohort Study. Prevention and Incidence of Asthma and Mite Allergy. *Clin Exp Allergy* 2001;31:576–581.
- Strachan DP: Family size, infection and atopy: The first decade of the 'hygiene hypothesis'. *Thorax* 2000;55(suppl 1):S2–S10.
- von Mutius E, Fritzsche C, Weiland SK, Roll G, Magnussen H: Prevalence of asthma and allergic disorders among children in united Germany: A descriptive comparison. *BMJ* 1992;305:1395–1399.
- von Mutius E, Weiland SK, Fritzsche C, Duhme H, Keil U: Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany. *Lancet* 1998;351:862–866.
- Braback L, Breborowicz A, Julge K, Knutsson A, Riiikjarv MA, Vasar M, Björkstén B: Risk factors for respiratory symptoms and atopic sensitisation in the Baltic area. *Arch Dis Child* 1995;72:487–493.
- Ursin G, Wu AH, Hoover RN, West DW, Nomura AM, Kolonel LN, Pike MC, Ziegler RG: Breast cancer and oral contraceptive use in Asian-American women. *Am J Epidemiol* 1999;150:561–567.
- Gruber C, Illi S, Plüth A, Sommerfeld C, Wahn U: Cultural adaptation is associated with atopy and wheezing among children of Turkish origin living in Germany. *Clin Exp Allergy* 2002;32:526–531.
- Kabesch M, Schaal W, Nicolai T, von Mutius E: Lower prevalence of asthma and atopy in Turkish children living in Germany. *Eur Respir J* 1999;13:577–582.
- Koopman LP, Wijga A, Smit HA, de Jongste JC, Kerkhof M, Gerritsen J, Vos AP, van Strien RT, Brunekreef B, Neijens HJ: Early respiratory and skin symptoms in relation to ethnic background: The importance of socioeconomic status; the PIAMA study. *Arch Dis Child* 2002;87:482–488.
- Hjern A, Haglund B, Hedlin G: Ethnicity, childhood environment and atopic disorder. *Clin Exp Allergy* 2000;30:521–528.
- Steenberg PA, Janssen NA, de Meer G, Fischer P, Nierkens S, van Loveren H, Opperhuizen A, Brunekreef B, van Amsterdam J-GC: The relationship between exhaled NO, respiratory symptoms, lung function, bronchial hyper-responsiveness and blood eosinophilia in a random sample of school children. *Thorax* 2003;58:242–245.
- Steenberg PA, Nierkens S, van Loveren H, van Amsterdam JGC: A simple method to sample exhaled NO not contaminated by ambient NO from children and adults in epidemiological studies. *Nitric Oxide* 2000;4:168–174.
- Kharitonov SA, Alving K, Barnes PJ: Exhaled and nasal nitric oxide measurements: Recommendations. The European Respiratory Society Task Force. *Eur Respir J* 1997;10:1683–1693.

- 20 Recommendations for standardized procedures for the on-line and off-line measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide in adults and children – 1999. This official statement of the American Thoracic Society was adopted by the ATS Board of Directors, July 1999. *Am J Respir Crit Care Med* 1999;160:2104–2117.
- 21 van Amsterdam JG, Verlaan AP, van Loveren H, Vos SG, Opperhuizen A, Steerenberg PA: The balloon technique: A convenient method to measure exhaled NO in epidemiological studies. *Int Arch Occup Environ Health* 1999; 72:404–407.
- 22 Steerenberg PA, Snelder JB, Fischer P, Vos JG, van Loveren H, van Amsterdam JGC: Increased exhaled nitric oxide on days with high outdoor air pollution is of endogenous origin. *Eur Respir J* 1999;13:334–337.
- 23 van Strien RT, Koopman LP, Kerkhof M, Oldenwening M, de Jongste JC, Gerritsen J, Neijens HJ, Aalberse RC, Smit HA, Brunekreef B: Mattress encasings and mite allergen levels in the Prevention and Incidence of Asthma and Mite Allergy study. *Clin Exp Allergy* 2003;33:490–495.
- 24 van Amsterdam JGC, Janssen NA, de Meer G, Fischer P, Nierkens S, van Loveren H, Opperhuizen A, Steerenberg PA, Brunekreef B: The relationship between exhaled nitric oxide and allergic sensitization in a random sample of school children. *Clin Exp Allergy* 2003;33:187–191.
- 25 Franklin PJ, Taplin R, Stick SM: A community study of exhaled nitric oxide in healthy children. *Am J Respir Crit Care Med* 1999;159: 69–73.
- 26 Ho LP, Wood FT, Robson A, Innes JA, Greening AP: Atopy influences exhaled nitric oxide levels in adult asthmatics. *Chest* 2000;118: 1327–1331.
- 27 Alders M: Fertility of foreign women: Extracting longitudinal information from stock data. *Maandstat Bevolking* 2000;48:9–11.