

Asthma and allergy in Albania and the UK

Alfred Priftanji, David Strachan, Michael Burr, Juventila Sinamati, Anila Shkurti, Edi Grabocka, Balvinder Kaur, Stephen Fitzpatrick

In the first phase of the International Study of Asthma and Allergies in Childhood, a large difference in occurrence of asthma symptoms was seen between children in Albania and the UK. We did skin-prick tests with various allergens and measured peak expiratory flow rate in about 1000 children from each country. A large difference in the proportion of exercise-induced bronchial reactivity was evident between children from Albania and the UK (0.8% vs 5.4%, respectively). However, the frequency of allergic sensitisation was closely similar (15.0% vs 17.8%, respectively). These results suggest that large geographical variations in asthma prevalence can arise without differences in frequency of atopy.

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Large worldwide differences in the prevalence of self-reported^{1,2} and parentally reported² symptoms of asthma and allergy emerged from the first phase of the International Study of Asthma and Allergies in Childhood (ISAAC). These global variations have stimulated substantial interest, but interpretation of their significance has not been straightforward because systematic differences in awareness, reporting, or labelling of symptoms could have arisen from linguistic and cultural diversity between the countries. As part of the second phase of ISAAC, we compared asthma occurrence in two countries that were at the extremes of the worldwide distribution of asthma frequency in ISAAC phase one: Albania (low) and the UK (high). At age 13–14

years, wheezing in the past 12 months was reported by 3% of Albanian children compared with 32% of children throughout the UK. The relative differences were closely similar or increased for frequent or severe asthma symptoms.²

We used a common protocol to obtain objective evidence of atopic dermatitis, bronchial responsiveness, and allergic sensitisation in 9–11-year-old children from Tirana, Albania, and West Sussex, UK. All children in the relevant classes were chosen from a random sample of schools (ten in Tirana, 33 in West Sussex). We asked the children's parents to complete a written questionnaire, much the same as that used in the phase one ISAAC, to ascertain symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema. We sought written parental consent to examine the skin for flexural dermatitis,³ to assess bronchial responsiveness to an exercise challenge,⁴ and to do skin-prick tests with extracts of *Dermatophagoides pteronyssinus*, *D farinae*, cat fur, *Alternaria*, and mixed grass and tree pollens (ALK, Horsholm, Denmark). In Tirana, two additional allergens (olive and *Parietaria*) were included in the analysis.

Skin-prick tests were done with 1-mm flanged lancets and measured after 15 min. Weals with a diameter of 3 mm or greater were judged to be evidence of atopy. After training of participants by instruction and practice blows, peak expiratory flow rate (PEF) was measured three times immediately before, and 5 min after, a 6-min period of running. The maximum of each set of readings was used to calculate the percentage fall in PEF after exercise. Pulse rate was measured for 15 s immediately after completion of the run, as an indicator of the intensity of the exercise. Children receiving inhaler treatment for asthma (mainly in the UK) were tested, when possible, at least 6 h after their last dose of medication.

The response to the questionnaire survey was 95%

	Tirana, Albania	West Sussex, UK	Odds ratio (95% CI)
Symptoms			
Wheeze in past year			
0–3 attacks	46/1057 (4.4%)	102/1050 (9.7%)	0.4 (0.3–0.6)
4–12 attacks	3/1057 (0.3%)	50/1050 (4.8%)	0.1 (0.0–0.2)
>12 attacks	2/1057 (0.2%)	17/1050 (1.6%)	0.1 (0.0–0.5)
Woken with wheeze in past year	21/1057 (2.0%)	81/1049 (7.7%)	0.2 (0.1–0.4)
Wheeze limiting speech in past year	5/1057 (0.5%)	24/1045 (2.3%)	0.2 (0.1–0.5)
Wheeze during or after exercise in past year	36/1031 (3.5%)	160/1033 (15.5%)	0.2 (0.1–0.3)
Dry cough at night apart from colds in past year	84/1029 (8.2%)	163/1036 (15.8%)	0.5 (0.4–0.6)
Asthma			
Ever	28/1051 (2.7%)	211/1042 (20.2%)	0.1 (0.1–0.2)
Ever and currently on treatment	19/1051 (1.8%)	147/1042 (14.1%)	0.1 (0.1–0.2)
Rhinitis in past year			
Without colds	225/1041 (21.6%)	252/1050 (24.0%)	0.9 (0.7–1.1)
With itchy eyes	70/1041 (6.7%)	168/1050 (16.0%)	0.4 (0.3–0.5)
Hay fever ever	28/1039 (2.7%)	202/1035 (19.5%)	0.1 (0.1–0.2)
Eczema			
Itchy rash affecting flexures in past year	60/1037 (5.8%)	152/1049 (14.5%)	0.4 (0.3–0.5)
Persistent itchy rash throughout past year	21/1037 (2.0%)	63/1046 (6.0%)	0.3 (0.2–0.5)
Woken at night by itchy rash in past year	28/1037 (2.7%)	63/1044 (6.5%)	0.4 (0.3–0.7)
Eczema ever	19/1043 (1.8%)	284/1047 (27.1%)	0.1 (0.0–0.1)
Physical signs			
Visible flexural dermatitis	21/1006 (2.1%)	59/971 (6.1%)	0.3 (0.2–0.5)
PEF reduction after exercise			
≥10%	43/992 (4.3%)	107/902 (11.9%)	0.3 (0.2–0.5)
≥15%	8/992 (0.8%)	49/902 (5.4%)	0.1 (0.1–0.3)
Skin prick reaction ≥3 mm			
Any allergen	141/936 (15.0%)	150/841 (17.8%)	0.8 (0.6–1.1)
<i>D pteronyssinus</i>	93/936 (10.0%)	65/841 (7.7%)	1.3 (0.9–1.8)
<i>D farinae</i>	45/936 (4.8%)	43/841 (5.1%)	0.9 (0.6–1.4)
Cat fur	34/936 (3.6%)	35/841 (4.2%)	0.9 (0.5–1.4)
<i>Alternaria</i>	8/936 (0.9%)	1/841 (0.1%)	7.2 (0.9–58.1)
Mixed grass pollen	32/936 (3.4%)	90/841 (10.7%)	0.3 (0.2–0.5)
Mixed tree pollen	7/936 (0.7%)	24/841 (2.9%)	0.3 (0.1–0.6)
Olive*	21/936 (2.2%)	..	..
<i>Parietaria</i> *	7/936 (0.7%)	..	..

PEF=peak expiratory flow rate. *Only used in Albania; two children responded to these allergens only.

Table 1: **Symptoms and physical signs of allergic disease in Tirana, Albania, and West Sussex, UK**

	Tirana, Albania			West Sussex, UK			p value for interaction
	SPT positive*	SPT negative	Odds ratio (95% CI)	SPT positive*	SPT negative	Odds ratio (95% CI)	
Symptoms in past year							
Wheeze							
Any	13/136 (9.6%)	31/776 (4.0%)	2.5 (1.3–5.0)	56/150 (37.3%)	84/691 (12.2%)	4.3 (2.9–6.4)	0.18
≥4 attacks	2/136 (1.5%)	3/776 (0.4%)	3.9 (0.6–23.2)	27/150 (18.0%)	24/691 (3.5%)	6.1 (3.4–10.9)	0.63
Rhinitis with itchy eyes	8/135 (5.9%)	53/765 (6.9%)	0.8 (0.4–1.8)	82/151 (54.3%)	57/690 (8.3%)	13.2 (8.7–20.1)	<0.0001
Itchy rash affecting flexures	7/131 (5.3%)	46/765 (6.0%)	0.9 (0.4–2.0)	36/151 (23.8%)	89/688 (12.9%)	2.1 (1.4–3.3)	0.05
Physical signs							
Visible flexural dermatitis	4/140 (2.9%)	16/769 (2.1%)	1.4 (0.5–4.2)	22/151 (14.6%)	34/693 (4.9%)	3.3 (1.9–5.8)	0.15
PEF reduction after exercise							
≥10%	6/135 (4.4%)	31/760 (4.1%)	1.1 (0.5–2.7)	27/137 (19.7%)	68/650 (10.5%)	2.1 (1.3–3.4)	0.19
≥15%	1/135 (0.7%)	7/760 (0.9%)	0.8 (0.1–10.2)	14/137 (10.2%)	27/650 (4.2%)	2.6 (1.3–5.2)	0.24

SPT=skin-prick test. PEF=peak expiratory flow rate. *≥3 mm weal to one or more allergens.

Table 2: **Selected symptoms and physical signs of allergic disease by skin-prick test response in each centre**

(1057/1114) in Tirana and 79% (1063/1346) in West Sussex. Table 1 shows the results of the parental questionnaire, and confirms large and highly significant variations in symptom occurrence between the two countries, as reported for children aged 13–14 years.^{1,2} Like the phase one ISAAC, severe forms of wheezing were especially uncommon in Tirana, and this pattern was mirrored with the results of the exercise challenge. The mean pulse rate after exercise was closely similar in children from Tirana and West Sussex (165 [SD 16] vs 167 [17] beats per min, respectively), and was similar to previous studies using this protocol.⁴

Eczema and its characteristic symptom, flexural rash, was less common in Albanian children than in children from the UK, which is consistent with the three-fold difference in occurrence of visible flexural dermatitis at examination (table 1). In contrast, the prevalence of allergic sensitisation differed little between children from Albania and the UK, although Albanian children were more likely to be sensitised to *D pteronyssinus* and *Alternaria* than UK children, who were more likely to react to grass and tree pollens (table 1).

Table 2 shows the association between positive skin tests (atopy) and indicators of allergic disease in the two countries. Wheezing, especially frequent attacks, was associated with atopy in both centres, but exercise-induced bronchospasm was related to skin-prick test responses in the UK only. A strong association of atopy with rhinoconjunctivitis and flexural dermatitis was seen in the UK, but not in Albania, although this difference was significant for rhinoconjunctivitis only (table 2).

Our findings confirm that there are substantial differences in asthma prevalence across Europe, which are unexplained by variations in occurrence of allergic sensitisation. Results comparing former socialist countries and western market economies have suggested an east–west variation in prevalence of allergic sensitisation around the Baltic Sea and within Germany.⁵ The similarity in occurrence of atopy in Albania and the UK was therefore unexpected. Our findings suggest that not all eastern European countries share a low rate of allergic sensitisation and add to evidence⁵ that challenges commonly held concepts of a deterministic association between atopy and asthma. Elucidation of the factors that protect Albanian children (with or without allergy) from development of asthma could point to new opportunities for prevention of respiratory morbidity in countries, such as the UK, with a high prevalence of this disease.

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asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet* 1998; **351**: 1225–32.

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Department of Allergy and Clinical Immunology, University Hospital Center “Mother Teresa”, Tirana, Albania (Prof A Priftanji FRCP, J Sinamati MD, A Shkurti MD, E Grabocka MD); **Department of Public Health Sciences, St George’s Hospital Medical School, London SW17 0RE, UK** (Prof D Strachan FRCP, B Kaur MPhM, S Fitzpatrick MSc); and **Department of Epidemiology, Statistics and Public Health, University of Wales College of Medicine, Cardiff** (M Burr FPhM).

Correspondence to: Prof David Strachan (e-mail: d.strachan@sghms.ac.uk)

Risk of venous thromboembolism with cyproterone or levonorgestrel contraceptives

Catherine Vasilakis-Scaramozza, Hershel Jick

Results of studies have shown that there is an excess risk of venous thromboembolism in users of oral contraceptives containing cyproterone compared with those containing levonorgestrel. We did a case-control study, in which we assessed the risk of idiopathic venous thromboembolism in women taking combined low-dose oestrogen oral contraceptives containing cyproterone (n=24 401) or levonorgestrel (n=75 000). We compared the 26 women in this population who had idiopathic venous thromboembolism with 144 matched controls. 12 individuals and 30 controls were taking contraceptives that contained cyproterone. Our results suggest that risk of venous thromboembolism is increased four-fold in women taking contraceptives containing cyproterone by comparison with those exposed to levonorgestrel.

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Results of several small studies suggest that individuals who take oral contraceptives containing cyproterone are at