

# Papers

## Changes in atopy over a quarter of a century, based on cross sectional data at three time periods

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Evidence that the prevalence of atopic diseases, including asthma and hay fever, has increased over the past 20-30 years comes mainly from questionnaire based surveys; objective measurements are limited.<sup>1-4</sup> We therefore measured serological markers of atopic sensitisation in stored serum samples that had been collected from a population of men over about 25 years.

### Participants, methods, and results

We used frozen ( $-40^{\circ}\text{C}$ ) serum samples from men aged 40-64 years who had attended the British United Provident Association (BUPA) Medical Centre, London, for a routine medical examination. An advantage of this cohort is its socioeconomic homogeneity—almost all were professionals or businessmen. We matched (by age and month of attendance) the 513 samples from men who attended during 1996-8 to samples from 513 men seen in 1981-2 and 513 seen in 1975-6. The serum samples had not previously been thawed; previous work has shown negligible decay in IgE during storage of serum.<sup>5</sup>

We first tested the samples using Phadiatop (Pharmacia & Upjohn), a standard qualitative serological marker of atopy based on a mixture of 11 common, inhaled allergens (grass, tree, nettle, mugwort, mould, and olive; cat, dog, and horse dander; and two house dust mites). The positive samples were then tested for specific IgE to grass (timothy grass), tree mix (elder, silver birch, hazel, oak, and plane), and cat dander (Pharmacia CAP system); we did not test the Phadiatop negative samples because Phadiatop includes all these allergens. The samples were also tested for IgG antibody to hepatitis A (DiaSorin) and to *Helicobacter pylori* (samples from 1996-8 only; Axis-Shield Diagnostics).

The table shows that we found highly significant increases over time in the proportion of men positive to Phadiatop and with specific IgE to the three inhaled allergens. The average rate of increase was equivalent to an additional 4.5% of men becoming Phadiatop positive each decade.

We compared the data on men born in 1932-42 who had had serum taken in the earlier periods (1975-6 or 1981-2, at age 40-50) and on men born in the same years (1932-42) who had had serum taken in the later period (1996-8, at age 54-64). The proportion of samples positive to Phadiatop were similar for both the earlier and later periods (35% and 34% respectively). The proportions of samples positive for specific IgE to grass, tree, and cat dander were also similar for the two time periods. In multiple regression, year of birth was associated with the prevalence of atopy ( $P < 0.001$ ), but current age was not.

Our results do not support previous data suggesting an inverse association between two common enteric infections and adult atopy. The proportion of samples that were Phadiatop positive was similar in men with and without serological evidence of past hepatitis A infection (37% *v* 34%) and *Helicobacter pylori* infection (40% *v* 36%). Two other markers of childhood infection available from questionnaire data—number of siblings and whether a man went to boarding school—also showed no association with Phadiatop positivity.

### Comment

Our data show that atopy in middle aged men has increased during the last quarter of the 20th century and that the prevalence of atopy does not decline with increasing age; rather, more recent birth cohorts are more likely to have become atopic. Reports of increases over time in specific IgE to inhaled allergens in adults from Nordic countries and Swiss and Japanese schoolchildren<sup>1-4</sup> involved younger subjects and shorter time periods than ours.

The reason for the increase in atopy is unknown. Our data suggest that it is unlikely to be an increased exposure to specific allergens (because sensitivity to both indoor and outdoor allergens increased). Our results also do not support the increase being due to declining childhood infections.

Proportions of men aged 40-64 years positive to Phadiatop\* and with specific IgE to three inhaled allergens, in three time periods,† and mean annual increase in prevalence. Values are percentages (95% confidence interval)

Year	Phadiatop	Grass	Tree	Cat
1975-6	30 (26 to 34)	16 (13 to 19)	5.7 (3.8 to 8.0)	4.1 (2.6 to 6.2)
1981-2	33 (29 to 37)	18 (14 to 21)	5.1 (3.3 to 7.3)	4.5 (2.9 to 6.6)
1996-8	42 (37 to 46)	27 (23 to 31)	12.6 (9.9 to 15.8)	10.1 (7.6 to 13.1)
Mean absolute annual increase in prevalence (%)‡	0.45 (0.17 to 0.73)	0.53 (0.30 to 0.77)	0.36 (0.19 to 0.53)	0.25 (0.13 to 0.38)

Test for trend ( $\chi^2$ ) was  $P < 0.001$  for Phadiatop and for each of the three allergens.

\*Preparation of 11 common, inhaled allergens used as a serological marker of atopy.

†In each time period there were 513 age matched men.

‡From logistic regression.

### What is already known on this topic

The prevalence of atopic diseases is increasing

Cross sectional studies show that the prevalence of atopy decreases with increasing age

### What this study adds

Serological measurements at three time periods provide objective evidence that earlier birth cohorts were less likely to have become atopic than more recent ones; this accounts for the apparent decreasing prevalence of atopy with age

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- 1 Nakagomi T, Itaya H, Tominaga T, Yamaaki M, Hisamatsu S-I, Nakagomi O. Is atopy increasing? *Lancet* 1994;343:121-2.
- 2 Linneberg A, Nielsen NH, Madsen F, Frølund L, Dirksen A, Jørgensen T. Increasing prevalence of specific IgE to aeroallergens in an adult population: two cross-sectional surveys 8 years apart: the Copenhagen allergy study. *J Allergy Clin Immunol* 2000;106:247-52.
- 3 Krause TG, Koch A, Firborg J, Poulsen LK, Kristensen B, Melbye M. Frequency of atopy in the Arctic in 1987 and 1998. *Lancet* 2002;360:691-2.
- 4 Kosunen TU, Høök-Nikannet J, Salomaa A, Sarna S, Aromaa A, Haahtela T. Increase of allergen-specific immunoglobulin E antibodies from 1973 to 1994 in a Finnish population and a possible relationship to *Helicobacter pylori* infections. *Clin Exp All* 2002;32:373-8.
- 5 Potts J, Luczynska C, Chinn S, Jarvis D, Burney P. Comparison of IgE measurements using the Pharmacia CAP systems in the European community health surveys I and II. *Eur Respir J* 2002;20(suppl 38):120S.  
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