House dust mite sensitivity in childhood asthma

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SUMMARY The clinical features of perennial asthmatic children with a skin or bronchial reaction to the house dust mite (*Dermatophagoides pteronyssinus*) were compared with those of asthmatic children without mite sensitivity. Mite sensitive asthma was characterised by an early age of onset of symptoms, these being predominantly nocturnal. A history of wheezing precipitated by dust exposure, during vacuuming, bedmaking, or dusting was present in 52% of cases. Asthmatic children with mite sensitivity were more likely to have been born at the time of the year when mite counts were highest. This was consistent with the idea that allergy may be associated with a period of susceptibility to sensitisation in early infancy.

Asthma precipitated by exposure to dust has been recognised for three centuries (Van Helmont, 1662), but the link between house dust and house mite allergy in asthmatic patients was not described until 1964 (Voorhorst *et al.*). Skin tests (Morrow-Brown and Filer, 1968), bronchial provocation tests (Aas, 1970), *in vitro* tests measuring IgE antibodies (Stenius and Wide, 1969), and histamine release from leucocytes (McAllen *et al.*, 1970) have clearly indicated that the mite, *Dermatophagoides pteronyssinus*, is one of the commonest allergens in Europe to which asthmatic patients are sensitised.

Sensitivity to *D. pteronyssinus* is common in childhood asthma (Sarsfield, 1974) but little has been published on the characteristics of such an allergy. The clinical importance of any one allergy in an asthmatic child with multiple allergen sensitivities can ultimately only be determined by history. There is an impression of an association between nocturnal asthma occurring throughout the year and house mite sensitivity, but this has not been established. Therefore, we have compared aspects of the clinical history of asthmatic children with and without a skin or bronchial reaction to *D. pteronyssinus*.

Patients and methods

Eighty-five children (62 boys and 23 girls) with moderate to severe perennial asthma, aged between 5 (the minimum for performing bronchial provocation tests adequately) and 14 years were studied.

Bronchial asthma was diagnosed by clinical and laboratory evidence of intermittent airways obstruction, reversible to a degree by bronchodilators. All the children had at least 6 moderately severe attacks of wheezing each year and their asthma was not satisfactorily controlled on bronchodilators alone.

The children were admitted to hospital for at least 48 hours. A full clinical history and examination was recorded on a standard questionnaire. Each had prick skin tests on the forearms to 10 allergens and a control solution. The reactions were measured after 20 minutes using a gauge, and weals of 2 mm diameter or greater were recorded as positive. The children had a bronchial provocation test to soluble extracts of *D. pteronyssinus*, using the method described by Warner (1976).

The medical notes of a further 163 unselected asthmatic children were studied to abstract information on skin test responses, date of birth, age of onset of wheezing, and the presence of nocturnal attacks.

Statistical analyses used the χ^2 test with continuity correction.

Results

Sixty-nine (81%) of the 85 children had a positive bronchial provocation test (BPT) to *D. pteronyssinus* and were designated as mite sensitive. 16 had no bronchial response to this allergen and, of these, on whom further tests were made had positive bronchial reactions to other allergens (4 Timothy grass, 3 cat fur, 1 *Alternaria tenuis*, and 1 *Cladosporium herbarum*).

Skin test responses to 10 allergens in each group of patients are shown in Table 1. Only one patient had totally negative skin tests, but she had marked bronchial lability and a family history of allergic disease. All 8 patients with negative skin tests to *D. pteronyssinus* also had negative BPTs to this allergen, but 8 (11%) of the positive skin reactors had negative BPTs. Significantly more of the mite sensitive group reacted to house dust extract and feathers. Fewer mite sensitive children reacted to the moulds *Cladosporium* and *Aspergillus fumigatus*, but this was significant only for the latter allergen.

Equal numbers of patients in each group had at least one first-degree relative with asthma, eczema, or hay fever. Both eczema and perennial rhinitis were more common in the mite sensitive group but this did not reach significance. 36 (52%) of 69 mite sensitive children had a clear history of asthma precipitated by exposure to dust during dusting, vacuuming, or bed-making compared with 3 (19%) of 16 in the mite negative group (Table 2).

Some studies were done retrospectively and of 163 asthmatic children, 120 (74%) had positive skin tests to *D. pteronyssinus*. The mite positive children gave a history of frequent nocturnal wheezing significantly more often (102 of 120) than did the mite negative group (18 of 43; χ^2 28.15, $P < 0.0005$).

As there were too few mite negative patients from the BPT for some analyses, they were grouped with 40 children who had negative skin tests to the mite from the retrospective study. The appropriate information was not available for the remaining 3 patients with negative skin tests to the mite from

that study. It is reasonable to assume that children with negative skin tests to the mite would also have a negative BPT to this allergen, as the association between negative skin tests and BPTs is at least 95% (Spector and Farr, 1974; Bryant *et al.*, 1975).

Significantly more of the mite sensitive children were born between July and December than at other times, and more mite sensitive patients had developed asthma before the age of 2 than the mite non-sensitive patients (Table 3). The Figure shows the

Figure Month of birth of children with mite-sensitive asthma or asthma without mite sensitivity compared with the Registrar General's mean figures for total live births each month for 1964 to 1974.

Table 1 Number of positive prick skin test reactions to 10 allergens in asthmatic children with and without a bronchial sensitivity to the house dust mite (*Dermatophagoides pteronyssinus*); the χ^2 and P values for the associations of the reactions to each skin test with bronchial challenge response to mite are given

Bronchial challenge to mite	No. of positive prick skin tests									
	<i>D. pteronyssinus</i>	House dust extract	Feathers	Cat	Milk	Timothy grass	Cocksfoot	<i>A. tenuis</i>	<i>C. herbarum</i>	<i>A. fumigatus</i>
Positive (69)	69	64	52	49	14	42	40	17	19	11
Negative (16)	8	10	6	10	5	12	11	6	8	8
χ^2	—	8.04	6.93	0.13	0.38	0.59	0.26	0.53	2.08	6.83
P	—	<0.005	<0.01	NS	NS	NS	NS	NS	NS	<0.01

NS = Not significant $P > 0.05$.

Table 2 Aspects of the clinical histories in children with and without a bronchial reaction to the house dust mite

	First-degree family history of atopy*		Eczema		Perennial rhinitis		History of dust exposure	
	+	—	+	—	+	—	+	—
Mite sensitive	38	31	40	29	40	29	36	33
Mite insensitive	9	5	7	9	6	10	3	13
χ^2	0.11		0.57		1.45		4.58	
P	NS		NS		NS		<0.05	

* 2 mite insensitive patients adopted, so family history not available.

Table 3 Age at onset of symptoms and month of birth of asthmatic children with a bronchial reaction to the house dust mite compared with asthmatic children with negative skin or bronchial provocation tests to the mite

	Age at onset of symptoms of asthma		Month of birth	
	< 2 years	> 2 years	January-June	July-December
Mite sensitive	44	25	24	45
Mite insensitive	19	37	31	25
χ^2		9.85		4.51
P		<0.005		<0.05

months of birth compared with the Registrar General's figures for total live births with peaks in April to May, and December to January. The mite sensitive children were born in greater numbers from August to December, when there were fewer live births.

Discussion

The children for the BPT study were carefully selected as having severe perennial asthma. The male to female ratio of 2.7:1 was similar to that found by McNicol and Williams (1973) in their severe asthmatics. Over half had at least one first-degree relative with an atopic disease, usually a parent. Few accurate figures of the incidence of allergy in families of asthmatic patients are available. Smith (1974) found that 87% of allergy clinic children had positive family histories, but he did not distinguish first-degree relatives from others.

Sarsfield (1974) found a 23% incidence of wheezing precipitated by dust exposure in 133 unselected asthmatic children and concluded that history was of limited use, but the analysis did not separate mite sensitive and insensitive children. We found that a positive history of wheezing on dust exposure strongly suggested mite sensitivity, and this indicates that such a history is useful for identifying perennial asthmatics with mite sensitivity.

Nocturnal wheezing was significantly more common in the children with skin hypersensitivity to the mite than in those without this allergy. *D. pteronyssinus* is found most often in mattress dust and bedding, so nocturnal symptoms may be expected to predominate in asthmatics sensitive to this allergen. It confirms the uncontrolled observation of Morrison Smith (1970) that 82% of asthmatic children with skin test mite sensitivity often had nocturnal attacks and had little seasonal variation in frequency of symptoms.

The high incidence of asthma deaths in the early morning (Cochrane and Clark, 1975) has prompted a reinvestigation of nocturnal and early morning wheezers (Hetzel *et al.*, 1977). The explanation is not clear, but there may be a circadian variation in airway calibre which makes wheezing more likely to

occur after allergen provocation during the night (Gervais *et al.*, 1977). Our data suggest that mite sensitivity may be an important factor in nocturnal asthma at least in childhood.

A high proportion of children with positive results to the BPT had other manifestations of allergic disease, 55% with eczema, 54% perennial rhinitis, 12% hay fever, and 16% urticaria. Nasal symptoms are common in childhood asthma (Viner and Jackman, 1976), and the histories suggested that these symptoms contributed significantly to our patients' overall disability. The slightly increased prevalence of perennial rhinitis in the mite sensitive children suggests that this may be another manifestation of mite allergy, although this would require confirmation by nasal challenge tests.

There is no large series of mite BPTs in asthmatic children but Aas (1970) reported that 53% of unselected asthmatic children had positive reactions after BPTs to house dust extract. House dust and mite extracts are not strictly comparable, but the correlation of positive reactions to the two allergens is good (Voorhorst *et al.*, 1969). It is possible that our higher incidence of positive BPT reactions to mite may result from the fact that our patients had more severe perennial asthma. An early age of onset of wheezing in the study by McNicol and Williams (1973) was associated with more severe disease and our mite sensitive children more often developed symptoms before 2 years of age than the mite nonsensitive children. This provides further indirect evidence that mite sensitive asthma is severe.

The children who had BPTs to *D. pteronyssinus* reacted to a variety of allergens on skin testing. As mite is the principal component of house dust extract (Voorhorst *et al.*, 1964), it is not surprising that more mite sensitive children reacted to house dust extract. It is interesting that more also reacted to feathers. Wormald (1971) suggested that reactions to feathers were caused by mite-allergens in the extract, possibly poultry mites with cross-reactivity with the house dust mite. Fewer mite sensitive children reacted to *A. fumigatus*. As the patients were selected with perennial asthma perhaps the perennial cause in the mite insensitive patients was the mould allergy.

The different distribution of month of birth between the 2 groups of asthmatics was striking. A comparison with total live births each month showed that the different distribution of month of birth of the mite sensitive children was a genuine one, and not due to general trends in month of birth. Other studies have demonstrated some inconclusive differences of birth season in patients with mite sensitivity in a small prospective study (Soothill *et al.*, 1976); seasonal or perennial symptoms (Pearson *et al.*, 1977); and skin test reactions to mixed allergen preparations (Björkstén and Suoniemi, 1976). This study is the first to show clear differences in month of birth in asthmatic children with an accurately identified allergy to *D. pteronyssinus*.

The largest number (26) of mite sensitive asthmatics were born in the quarter October to December and the smallest (9) in April to June. These quarters correspond respectively to the finding of the highest and lowest frequencies of live mites in house dust (Blythe, 1976). The development of allergy may be associated with a period of susceptibility to sensitisation in early infancy. This was suggested by Taylor *et al.* (1973) who demonstrated an association between the delayed development of serum IgA in infants who subsequently had eczema and positive results to skin tests. This idea is supported by the data presented, with mite sensitive asthmatic children being born at times when they would have a high mite exposure during their early months of maximum susceptibility to sensitisation.

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