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Nasal allergy to avian antigens

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Summary

This study describes the case of a patient who developed symptoms of rhinoconjunctivitis on exposure to budgerigars and parrots. An IgE-mediated allergy to budgerigar, parrot and pigeon antigens was demonstrated using both *in-vivo* challenge tests (skin and nasal provocation tests) and *in-vitro* investigations (radio-allergo-sorbent test, histamine release test). The study shows that the development of nasal disease can be associated with allergy to avian antigens.

Introduction

The development of hypersensitivity pneumonitis in bird fanciers is well known. The disease was first described in pigeon breeders in 1965 by Reed *et al.* [1]. Exposure to other birds may also induce this disease [2–5]. Type III and type IV allergic reactions may be involved [6]. There is evidence that IgE-mediated mechanisms may also play a role in allergy to bird-derived materials [7–9]. Isolated nasal allergy to avian antigens has rarely been reported. To our knowledge only Pelikan & Pelikan-Filipek [10] have analysed the nasal complaints in pigeon breeders.

Subject and methods

Mrs D, female, 47-years-old, had a history of perennial rhinoconjunctivitis. Symptoms of running nose, sneezing and itching of the eyes had started 7 years previously and had gradually become worse. She had chronic symptoms with acute aggrevation immediately after contact with the budgerigar and the parrot, which she had been keeping for 8 years outside the house. This exacerbation continued for about 24 hours. She had no symptoms after contact with her pigeons. The history revealed no other provoking allergens. Other stimuli were non-specific (tobacco smoke, painty smell and fog). She

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Table 1. Intradermal skin tests

	Concentration				
	0·00025	0·0025	0·025	0·25	mg/ml (feather extract)
Allergen	10^{-8}	10^{-7}	10^{-6}	10^{-5}	v/v (pigeon serum)
Budgerigar feather	±	±	+	+++	
Parrot feather	+	+	++	++	
Pigeon serum	−	+	++	++	

Skin test response of patient D., expressed according to the grading system of Norman [11]. − Represents an erythema and weal of < 5 mm each: ± reaction: erythema and weal of 5–10 mm each; + reaction: erythema of 11–20 mm and weal of 5–10 mm: ++ reaction: erythema of 21–30 mm and weal of 5–10 mm: +++ reaction: erythema of 31–40 mm and a weal of 10–15 mm or with pseudopods; ++++ reaction: erythema > 40 mm and weal > 15 mm or many pseudopods.

had never experienced atopic dermatitis. No features of bronchial asthma or hypersensitivity pneumonitis were present. Spirometry, bronchial provocation with histamine and a chest X-ray gave normal results. There was marked blood eosinophilia ($0{\cdot}673 \times 10^9$ cells/litre).

Allergens

Lyophilized budgerigar and parrot feather extracts and lyophilized pigeon serum were obtained from Diephuis Laboratorium, Groningen, The Netherlands.

Skin tests

Dilutions of budgerigar and feather extracts (0·25, 0·025 and 0·0025 mg/ml) and dilutions of pigeon serum (10^{-5}, 10^{-6}, 10^{-7} and 10^{-8} v/v) were made using extract reconstituted in phosphate buffered saline (PBS) containing HSA 0·03% and phenol 0·5%. Intradermal skin tests were performed and reactions were read after 20 min using the grading system of standardized plus signs, devised by Norman [11].

Nasal provocation tests

Lyophilized feather extract and serum were reconstituted with PBS containing HSA 0·03% and benzalkonium chloride 0·5%. After nasal provocation with 0·2 ml PBS in each nostril, dilutions of parrot or budgerigar feather extract (from 0·025 to 2·5 mg/ml in ten-fold steps), pigeon serum (from 10^{-5} to 10^{-2} v/v in ten-fold steps) or histamine chloride (in dilutions of 0·25 and 0·5 mg/ml) were sprayed into each nostril using a deVilbiss atomizer connected to a pressure pump. The allergens were applied at 15-min intervals and histamine chloride at 10-min intervals. All tests were performed on separate days.

Total nasal airway resistance (NAR) was measured and calculated using a passive anterior rhinomanometer (Heyer Parr) as described by Clement *et al.* [12]. Sneezes were counted and secretion was collected as described by Borum [13].

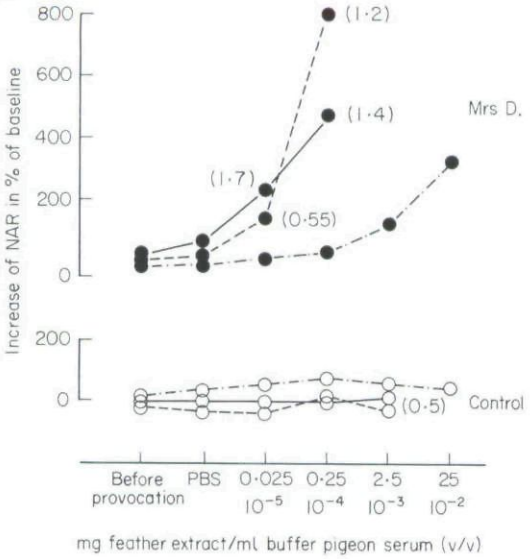

Fig. 1. Increase in nasal resistance, expressed as percentage of the baseline value, induced by nasal provocation with allergen extract in Mrs D. (●) and a non-atopic control (○). Dose–response curves are constructed for budgerigar feather extract (●— — —●), parrot feather extract (●——●) and pigeon serum (●—·—·—●). When a measurable amount of secretion was produced, the amount in ml is included in parentheses.

Total IgE and allergen-specific IgE

Total IgE was determined using IgE RIA (Pharmacia, Uppsala, Sweden), according to the manufacturer's instructions. Allergen-specific IgE was determined by a radio-allergo-sorbent test using agarose beads as allergen support. Bird allergens were prepared and coupled to CNBr-activated Sepharose 4B as described previously [9].

Precipitating antibodies

Precipitating antibodies against feather extract from budgerigar and parrots, and against serum from pigeons, were determined by double diffusion using the method described by Ouchterlony [14].

Histamine release from washed leucocytes

Incubation of washed leucocytes with allergen extracts (budgerigar feathers, parrot feathers and pigeon serum) and assay of histamine released into the supernatant, were performed using Siraganian & Hook's method [15] as described previously [9].

Results

Skin tests

Intradermal skin tests with extracts of house dust mites, pollens, animal danders and moulds were negative. Mrs D showed immediate type skin reactions to both budgerigar and parrot feather extract and to pigeon serum (Table 1). Non-specific effects of the extracts could be excluded as three non-atopic controls showed no skin reactivity to the avian antigens.

Table 2. IgE against avian antigens

	Budgerigar		Parrot		Pigeon		Total IgE
	Feathers	Serum	Feathers	Serum	Feathers	Serum	IU/ml
Serum	17	15	25	21	5	15	500

Serum from Mrs D. tested for the presence of IgE to budgerigar, parrot and pigeon feathers and serum. Results are expressed as binding of ^{125}I-anti-IgE.

Table 3. Test for non-specific binding to bird antigens

	Budgerigar		Parrot		Pigeon		Total IgE
	Feathers	Serum	Feathers	Serum	Feathers	Serum	IU/ml
1	1	0					355
2	1	0					1350
3			0	0			365
4			3	1			5500
5					0	0	540
6					0	0	700

Six sera with various total IgE levels were incubated with Sepharose-coupled avian antigens.

Table 4. IgE against parrot antigens

	Parrot		Total IgE
Patient	Feathers	Serum	IU/ml
A.	9	0	1400
W.	15	1	450
Ro.	24	4	4000
Rij.	27	32	340

Sera from four patients showing specific IgE to parrot feathers and sera. The results are expressed as binding of ^{125}I-anti-IgE.

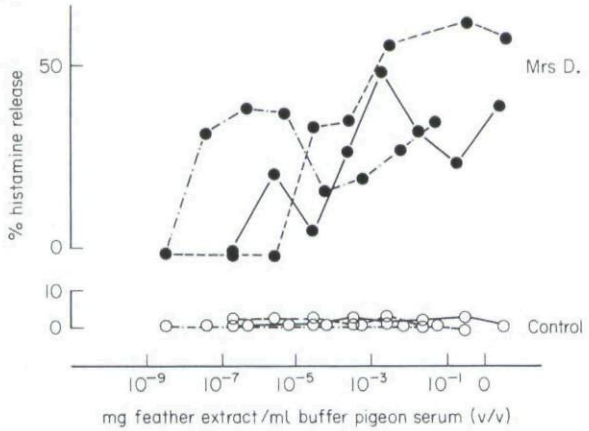

Fig. 2. Histamine release from leucocytes from Mrs D. (●) and from a non-atopic control (○) on incubation with budgerigar feather extract (●– – –●), parrot feather extract (●——●) and pigeon serum (●—·—●).

Nasal provocation tests

A marked increase of NAR was seen after provocation with avian antigens (Fig. 1). This nasal response could not be induced in a non-atopic control, indicating that the bird-derived materials that we used had no irritating effect on the nose. Histamine chloride (0·25 mg/ml) caused an increase in NAR of 175% of the baseline value and produced 0·75 ml of secretion.

Total IgE and allergen-specific IgE

Serum obtained from the patient was tested for the occurrence of total and allergen-specific IgE. IgE against all feather extracts and the corresponding bird sera was found (Table 2).

In order to exclude non-specific binding to bird antigens, control studies were carried out by testing sera with total IgE levels between 300 IU/ml and 1300 IU/ml. A binding of 0–3% was found (Table 3). Control studies of the budgerigar feather RAST are described elsewhere [9].

We looked for patient sera with IgE binding to parrot antigens to find out whether this was an isolated phenomenon. In patient sera sent from other departments in the period 1984–1986 we found four sera containing IgE against parrot antigens (Table 4).

Precipitating antibodies

In Ouchterlony tests with serum from Mrs D., which was incubated with extracts of faeces or feathers or with serum from budgerigar, parrot or pigeon, there were either no precipitates or they were only weak.

Histamine release from washed leucocytes

The histamine release test showed that leucocytes obtained from the patient released histamine after incubation with budgerigar or parrot feather extract or pigeon serum, whereas a normal donor showed no release on exposure to these avian antigens (Fig. 2).

Discussion

Isolated nasal allergy to bird-derived antigens is uncommon. The literature on allergy to avian antigens has focused on the development of lung disease [1–7], especially on hypersensitivity pneumonitis [1–5]. Pelikan & Pelikan-Filipek [10] recorded a late nasal response to pigeon dropping challenge in 53% of pigeon breeders with nasal complaints. Based on the occurrence of precipitating IgG antibodies, general malaise, increased body temperature and a rise in white blood count, they suggested that a type III hypersensitivity reaction was involved.

The existence of IgE-mediated allergy has been established for budgerigars [7,9], canaries [9] and pigeons [8]. Type I allergy to parrot antigens seems to be uncommon, as it is only recently that a patient with an allergy to parrots and also egg yolk has been described [16]. The diagnosis of the allergy to the parrots was established by history and by RAST.

In this report we have demonstrated IgE against bird-derived material from several species. The findings of a recent study [9] suggest that budgerigar and canary feather extracts contain more different IgE binding antigens than the corresponding bird sera, as only patient sera containing high levels of IgE against bird feather extract react with bird serum. This is probably also true for parrot antigens, as all patient sera in this study (Tables 2 and 4) showed IgE binding in the parrot feather RAST that was higher than, or equal to, the corresponding serum RAST. However, the binding of IgE to pigeon feathers was less than the binding to pigeon serum. A possible explanation could be that a cross-reactivity exists between pigeon serum and other bird sera. It is also possible that we did not use an optimal allergen concentration in the pigeon feather RAST.

In the nasal provocation test, pigeon serum induced a significant nasal response (increase of NAR > 100%) in a concentration 10 000 times higher than the concentration needed for a 1+ skin reaction. The concentration of budgerigar feather extract needed to elicit a nasal response was 100 times the concentration needed for a 1+ skin reaction, while for parrot feather extract the concentration needed was equal to that for a 1+ skin reaction. This suggests that the sensitivity to pigeon antigen in the target organ, the nose, was lower than the nasal sensitivity to budgerigar and parrot antigens, which in fact corresponds with the patient's history.

In the nasal provocation test with histamine, Mrs D. reacted by producing a considerable amount of secretion when provoked with a low dose (0·25 mg/ml). We reported in a recent study that healthy non-atopic subjects do not show any nasal response after application of this concentration [17]. This suggests the occurrence of a non-specific nasal reactivity. Evidence for a relation between allergy and nasal hyperreactivity has been produced by Borum [18], who reported an increase in reactivity to histamine and methacholine in pollinosis patients during the pollen season.

We conclude that rhinitis in bird fanciers can be associated with an IgE-mediated allergy to bird antigens.

References

1 Reed CE, Sosmon AJ, Baree RA. Pigeon breeder's lung. J Am Med Assoc 1965; 193:261–5.

2 Korn DS, Florman AL, Gribetz I. Recurrent pneumonitis with hypersensitivity to hen litter. J Am Med Assoc 1968; 205:44–5.

3 Boyer RS, Klock LE, Schmidt CD *et al.* Hypersensitivity lung disease in the turkey-raising industry. Am Rev Respir Dis 1974; 109:630–5.

4 Cunningham AL, Fink JN, Schlueter DP. Hypersensitivity pneumonitis due to droves. Pediatrics 1976; 58:436–42.
5 Hargreave FE, Pepys J, Longbottom JL, Wraith DB. Bird breeder's (fanciers) lung. Lancet 1966; i:445–9.
6 Richardson HB. Hypersensitivity pneumonitis—pathology and pathogenesis. Clin Rev Allergy 1983; 1:464–86.
7 Faux JA, Wide C, Hargreave FE, Longbottom JL, Pepys J. Immunological aspects of respiratory allergy in budgerigar (*Melopsittacus undulatus*) fanciers. Clin Allergy 1971; 1:149–58.
8 Ebner H, Kraft O, Goetz M *et al.* Nachweis von IgE Antikörpern gegen Taubenserum und Taubenkot Komponenten mittels RAST. In: Kölner RAST Symposion 3:161–5 (Grosse, Berlin, 1981).
9 van Toorenenbergen AW, Gerth van Wijk R, van Dooremalen G, Dieges PH. Immunoglobulin E antibodies against budgerigar and canary feathers. Int Arch Allergy Appl Immunol 1985; 77:433–7.
10 Pelikan Z, Pelikan-Filipek M. A new disease: a nasal form of pigeon breeder's disease. Allergy 1983; 38:309–18.
11 Norman PS. Skin testing. In: Rose NR, Friedman H, eds. Manual of clinical immunology, 2nd edn. Washington: Am Soc for Microbiology, 1980:789–93.
12 Clement PAR, van Dishoeck EA, vd Wal RJ, Stoop AP, Hoeck GT, Van Strik R. The nose provocation and the passive anterior rhinomanometry (P.A.R.) Acta oto-rhinolaryngol Belg 1978; 32:56–63.
13 Borum P. Nasal metacholine challenge. J Allergy Clin Immunol 1979; 63:253–7.
14 Ouchterlony D. Antigen–antibody reactions in gels; types of reactions in coordinated systems of diffusion. Acta Path Microbiol Scand 1959; 32:231–40.
15 Siraganian RP, Hook WA. Histamine release and assay methods for the study of human allergy. In: Rose NR, Friedman H, eds. Manual of clinical immunology 2nd edn. Washington: Am Soc for Microbiology, 1980:808–21.
16 de Maat-Bleeker F, Van Dijk AG, Berrens L. Allergy to egg yolk possibly induced by sensitization to bird serum antigens. Ann Allergy 1985; 54:245–8.
17 Gerth van Wijk R, Dieges PH. Comparison of nasal response to histamine, methacholine and phentolamine in allergic rhinitis patients and controls. Clin Allergy 1987; 17: 563–570.
18 Borum P. Nasal reactivity in rhinitis. Eur J Respir Dis 1983; 64 (suppl 128): 65–71.