

# Allergy to feathers

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Skin prick test reactivity to commercial and self-made feather-allergen extracts was examined in 269 consecutive adult patients with suspected allergic cutaneous or respiratory symptoms who had been referred to a university clinic. Some 177 subjects reacted to any inhalant allergen. Twenty-four (9% of the whole group and 14% of those positive to any inhalant allergen) reacted to commercial feather extracts from ALK (Hørsholm, Denmark), and 51 to any of the seven feather extracts used. Feather-mix RAST (Pharmacia, Sweden) was positive in three cases only. Skin prick test or CAP-RAST or both to house-dust mite were positive in 16 of those 24 subjects positive to the commercial feather extracts, but in only 23 of the 150 other atopic subjects ( $P < 0.001$ ). A nasal challenge with a feather extract was made in 20 cases, always with negative result. In immunospot studies, concomitant allergy to feather-allergen extracts and house-dust mite could be demonstrated. Mite allergens in feather extracts were verified in RAST-inhibition studies. A clinically significant feather allergy was found in one patient only. The results suggest that true feather allergy is very rare, and most of the positive reactions seen in skin prick tests to feather extracts are probably caused by mite allergens present in feathers.

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Feathers have been reported to cause allergic asthma and rhinitis (1, 2), and possibly also atopic dermatitis (3). Duck, goose, and hen feathers are considered to be more important causes of IgE-mediated allergic reactions than the feathers of parrot, canary, or budgerigar (1, 4).

Bird breeder's lung (allergic alveolitis) is common in pigeon breeders. In most cases, IgG antibodies against birds' sera, feces, and feather proteins can be found in the patient's serum (5). Feather pillows, eiderdowns, and feathers used in artificial fishing flies are also possible causes of allergic alveolitis (6–9).

Positive results in intracutaneous and skin prick tests (SPT) with feather allergens have been reported in 20–60% of patients suspected to be allergic to feathers (10–12). The clinical relevance of these reactions has not been established. In asthmatic children with positive SPT results, von der Hardt & Meiser (12) were unable to provoke asthma in challenge with feather extracts.

We studied the occurrence of feather SPT positivity, its clinical relevance, and the relationships between feather exposure, SPT reactivity, and clinical symptoms.

## Material and methods

### Part I

The study population comprised 269 consecutive adult (>14 years of age) patients with suspected atopic allergic cutaneous or respiratory symptoms, who had been referred to the Skin and Allergy Hospital in Helsinki. Of them, 199 were women (mean age 33.5, range 15–78 years) and 70 men (mean age 32.1, range 15–62 years).

Routine SPT series were done on the ventral aspects of the lower arms with nine common inhalant allergens (birch, alder, timothy, *Alopecurus* and mugwort pollens, cat, dog, house-dust mite (HDM) (*Dermatophagoides pteronyssinus*, Der p), and *Cladosporium herbarum* and three feather-allergen solutions (duck, hen, and goose feathers), all from ALK (Allergologisk Laboratorium, Hørsholm, Denmark). The potency of the allergens was 10 HEP (histamine equivalent prick), except those of *Cladosporium* (1:20, w/v) and feathers (1:100, w/v). Histamine dihydrochloride, 10 mg/ml, was used as the positive and the diluent of the SPT materials as the negative control. Reactions at least 3 mm in diameter and larger than the negative control were

considered positive. The patient was classified as atopic if at least one positive SPT reaction to any of the nine inhalant allergens was seen. Some 177 patients (66%) met this criterion of atopy.

If any feather allergen produced a positive response in SPT, specific serum IgE was measured with feather multi-RAST (duck, goose, hen, and turkey) and HDM (Der p) CAP-RAST, both from Pharmacia (Uppsala, Sweden).

A questionnaire concerning the use of feather products and the occurrence of possible symptoms caused by them, exposure to pets, presence of wall-to-wall carpeting, and use of air cleaners was answered by all patients. Exposure to feathers was considered significant if the patient had ever used an eiderdown (down quilt) or a feather pillow for more than 1 year. The use of a down jacket or a down sleeping bag was regarded as a minor source of exposure.

## Part II

In this part of the investigation, only the adult atopic patients who reacted to any inhalant allergen in the SPTs with routine series in part I of the study were recruited. There were 133 women and 44 men, with the mean age of 29.5 years. Ninety-eight patients underwent SPT with feather extracts made in our own laboratory, and feather-mix RAST was performed on 50 patients' sera. HDM (Der p) SPT and/or HDM CAP-RAST were performed in all but three cases. The following feather sources were used for our own Finnish feather extracts for SPTs: duck and goose down before and after washing and other refining procedures was obtained from a Finnish down-processing unit (Suomen Höyhen Oy). The samples were extracted in 0.1 mol/l phosphate-buffer (pH 7.0 and 1:10, w/v) in a refrigerator overnight and filtered through Whatman no. 4 filter paper. The filtrates were then dialyzed against 20 mmol/l ammonium bicarbonate in a dialyzing tube with a cutoff point of 3.5 kDa for 3 × 24 h, and finally freeze-dried.

The freeze-dried extracts were then reconstituted with glycerosaline (50:50). SPTs were first performed with the "natural" down extract at various concentrations in 10 nonatopic control subjects and in 12 atopic subjects with respiratory symptoms. A 2% (w/v) "natural" goose down extract produced a 3-mm reaction in three of the 12 atopics, but in none of the 10 controls. This concentration was chosen for further skin testing with unrefined down. The test concentration of the refined down extracts was, correspondingly, 1% (w/v) in glycerosaline. However, the amounts of refined extracts were so small that only 33 patients could be tested.

An intranasal provocation test with aqueous goose-feather extract (Aquagen®, ALK) was performed on 14 patients, with duck-feather extract on four patients, and with hen-feather extract on two patients. Before the provocation, all the 20 patients subjected to provocation had been free of major airway symptoms for 1 month and were using neither topical nor systemic antiallergic drugs. Aquagen diluent was used as the negative control solution. If the control test in one nostril was negative, 0.05 ml of the active substance was sprayed into the other nostril. The results were estimated at 20–30 min as follows. Blocking of the nasal airway, change in the color of the nasal mucosa, and discharge were estimated on a scale of 0–2. More than five sneezes scored one point and symptoms in other organs (skin, lungs, eyes) also scored one point. A reaction of three or more points was regarded as positive (adaptation of the German recommendation [13]).

Feather-specific IgE was studied in the sera of 13 patients by the immunospot method (14). Two serum samples were from patients with a positive SPT to ALK feathers and with positive RAST to a feather mix (1.5 and 6.7 kU/l, respectively). Another serum sample was a mixture of sera from two patients with a positive SPT to Finnish feather extracts, but negative to ALK feathers. The third sample was a mixture of nine sera from patients with positive SPTs both to any ALK and any Finnish feather test solutions. The fourth sample was a serum pool from 20 HDM-allergic patients, the fifth was a pool from three HDM-negative atopic control patients, and the sixth was a serum pool from 20 nonatopic control patients.

Mite allergens in feather extracts were studied in RAST inhibition according to Yman et al. (15) with mite disks (Der p) from Pharmacia (Uppsala, Sweden) and a serum pool from 20 mite-allergic patients. Consecutive serial (1:2) dilutions from an ALK hen SPT solution and test solutions made from unrefined duck and goose feathers were used as inhibitors. An ALK mite SPT solution was used as the positive and a latex allergen extract as the negative control inhibitor.

Informed consent was obtained from every patient. The study was approved by the local ethical committee.

The statistical analysis was made by using Fisher's exact test when needed.

## Results

### Part I

The presence and number of pets, cage birds, wall-to-wall carpeting, and use of air cleaners did not

Table 1. Exposure to inhalant allergens in 177 atopic and 92 nonatopic subjects

|                                            | Atopic<br>% | Nonatopic<br>% |
|--------------------------------------------|-------------|----------------|
| > 1-year exposure to feathers <sup>a</sup> | 35          | 56             |
| Feather pillow at present                  | 12          | 19             |
| Down quilt at present                      | 7           | 12             |
| Exposure to any pet <sup>b</sup>           | 68          | 74             |
| Dog                                        | 41          | 52             |
| Cat                                        | 34          | 37             |
| Cage bird                                  | 14          | 13             |
| Other pets                                 | 26          | 13             |
| Wall-to-wall carpet in bedroom             | 2           | 5              |
| Air cleaner in bedroom                     | 10          | 4              |

<sup>a</sup> Over 1-year exposure to any feather product until time of study.

<sup>b</sup> At any time during life.

differ between the atopics and nonatopics (Table 1). Rhinitis, asthma, and dermatitis from contact with feathers were reported by atopics more often than by nonatopics (Fig. 1), and by women more often than by men (Fig. 2). The nonatopics were exposed to feathers more often than the atopics, but the differences for other allergens were minimal between these two groups.

A positive SPT to any ALK feather allergen was seen in 24 patients (9% of the whole group and 14% of those positive to any inhalant allergens); two reacted to duck feathers, 12 to goose, and 15 to hen feathers. RAST to a feather mix was positive in only two cases. SPT or RAST to HDM was positive in 16 of the 24 feather-positive patients, but in only 23 of the 150 other atopic subjects ( $P < 0.001$ ).

One patient with a moderately elevated feather-mix RAST value (6.7 kU/l) and positive SPTs to many feather extracts had not noticed any symp-

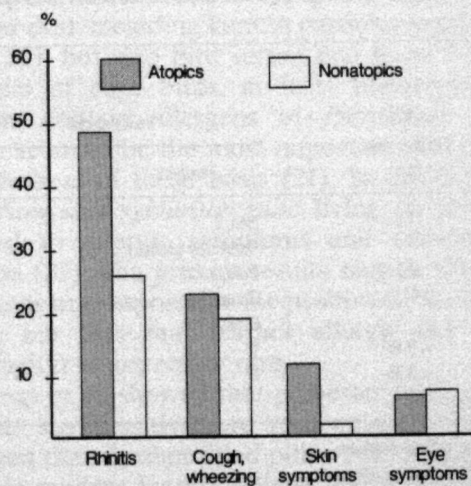


Fig. 1. Symptoms from feather exposure in 177 adult atopic and 92 adult nonatopic patients with respiratory symptoms.

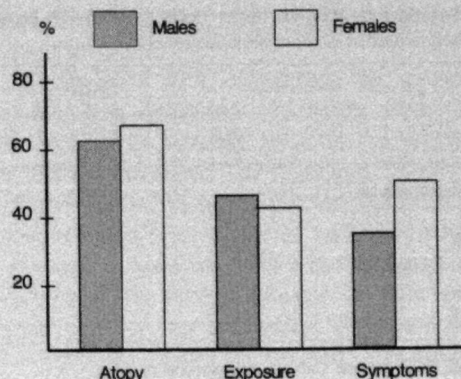


Fig. 2. Atopy, long-lasting (more than 1 year) exposure to feather products, and subjective symptoms from feathers and feather products in 70 male and 199 female patients with respiratory symptoms.

toms from feather products, nor did she react to a feather extract in a nasal challenge test. She had had a cage bird in her youth, she got allergic symptoms from hen's egg, and her hen's egg white RAST was 3.6 kU/l and hen's egg yolk RAST 2.6 kU/l. In a second patient, feather-mix RAST was 1.5 kU/l, and SPT to hen feather was positive, but the nasal challenge test was negative. She had allergic symptoms while using a feather pillow. She was also allergic to HDM. In her youth, she had often visited a henhouse.

## Part II

The SPT with any feather allergen was positive in 51 of the 177 (28%) atopic patients. SPT was positive to any of the ALK feather allergens in 24 of the 177 patients, to any of the Finnish unrefined feather extracts in 38 of 98 patients, and to any of the Finnish refined feather extracts in only four patients. The nasal challenge test was negative in all of the 20 patients tested.

A third feather-RAST-positive patient had a positive SPT result to HDM and the Finnish unrefined goose feather extract, but not to any other feather allergen solutions. He had a high feather RAST value (57 kU/l) and a high hen's egg white RAST (100 kU/l), and his total serum IgE was 10000 kU/l. Use of a feather pillow caused allergic symptoms, possibly due to allergens of feather or HDM.

HDM allergy was found in patients with a positive SPT to any feather allergen significantly more often than in the other atopic subjects (Table 2). Total feather-specific IgE in serum, measured by the immunospot method, was high in the two cases with a positive feather mix RAST (Fig. 3) and low in mixtures of two and nine sera, respectively, of patients with a positive feather SPT, but a negative

Table 2. Correlations of HDM and feather reactions among 177 atopic subjects showing positive reaction to any inhalant allergen in SPT

| SPT results              | HDM <sup>a</sup> |     | P value <sup>b</sup> |
|--------------------------|------------------|-----|----------------------|
|                          | Yes              | No  |                      |
| Any ALK feather allergen |                  |     |                      |
| Positive                 | 16               | 8   | <0.001               |
| Negative                 | 23               | 127 |                      |
| Any feather allergen     |                  |     |                      |
| Positive                 | 23               | 28  | <0.001               |
| Negative                 | 16               | 107 |                      |

<sup>a</sup> SPT and/or RAST positive. Data on three patients missing.<sup>b</sup> Fisher's exact test.

feather mix RAST (Table 3). In the latter serum pool, the HDM immunospot was positive (Fig. 3). A pool of HDM-positive control sera also reacted to feathers in the immunospot, while serum pools from other atopic and nonatopic subjects did not (data not shown).

In RAST inhibition, HDM allergen activity was high in the commercial ALK hen feather extract, causing a 65% inhibition of the mite RAST (Fig. 4). The inhibition was also marked in the extracts made from unrefined goose and duck feathers (Fig. 4). The inhibition with the homologous HDM was 70% and negative (<20%) with latex allergens (not shown).

## Discussion

Positive skin reactions to various commercial feather allergen preparations were seen in 14% of patients with respiratory symptoms suspected to be allergic. Symptoms from feathers were reported by 58% of feather SPT-positive patients and by 55%

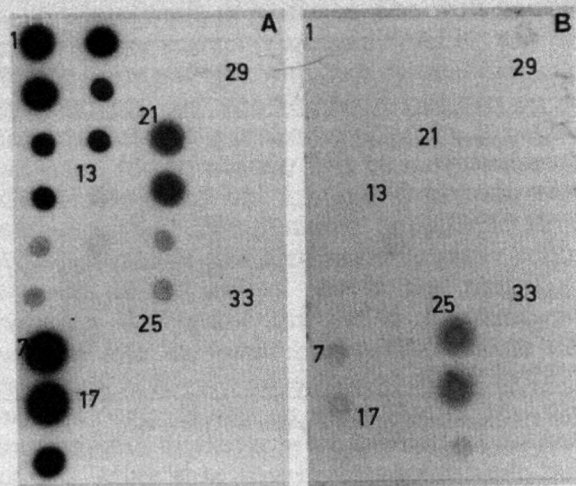


Fig. 3. IgE binding to unrefined (1, 7) and refined (29, 33) duck and goose extracts and to commercial allergens (13, hen; 17, goose; 21, duck; 25, Der p). Patient 2 from Table 3 had IgE to unrefined feathers (A), whereas sera from patients 5–13 contained IgE to mite and less to unrefined feathers (B).

of other SPT-positive atopics. This discrepancy between the SPT result and the subjective symptoms suggests that either the feather SPT allergens were of poor quality or people believe feather products to be potent allergens only on the basis of reputation.

Positive SPT reactions to Finnish extracts made from unrefined down were more frequent (38/98=39%) than reactions to the commercial extracts (15/98=15%), the difference being significant. Extracts made from refined down gave the fewest positive reactions (4/33=12%).

A positive correlation was seen in the SPT reactions to feather allergen preparations and

Table 3. Immunospot results (0–3) to feather SPT allergens (ALK duck, hen, and goose, and own unrefined and refined duck and goose extracts) and HDM (Der p). All immunospot tests with refined feather extracts were negative

| Patient no. | Positive feather SPTs |                                 |               | RAST Feather mix IU/l | Immunospot                                 |     |
|-------------|-----------------------|---------------------------------|---------------|-----------------------|--------------------------------------------|-----|
|             | ALK                   | Finnish feather extracts        |               |                       | Feathers                                   | HDM |
|             |                       | Unrefined                       | Refined       |                       |                                            |     |
| 1           | Hen                   | ND                              | ND            | 1.5                   | Hen 2<br>Unrefined goose 1                 | +   |
| 2           | Duck<br>Hen           | Duck<br>Goose                   | Negative      | 6.7                   | Duck 3<br>Goose 3<br>Others 1 <sup>a</sup> | —   |
| 3–4         | Negative              | Positive                        | Positive      | <0.35                 | 1 <sup>b</sup>                             | —   |
| 5–13        | Positive              | Positive in 5,<br>Negative in 4 | Negative in 9 | <0.35                 | 1 <sup>c</sup>                             | +   |

<sup>a</sup> One serum. Immunospot was positive to unrefined duck and goose and to ALK feathers, but not to refined feathers.<sup>b</sup> Mixture of two sera. Immunospot was positive to unrefined goose feathers, but negative to all other feather allergens.<sup>c</sup> Mixture of nine sera. Immunospot was positive to ALK hen and to unrefined duck and goose feathers, but negative to all other feather allergens.

SPT: skin prick test; ND: not done.

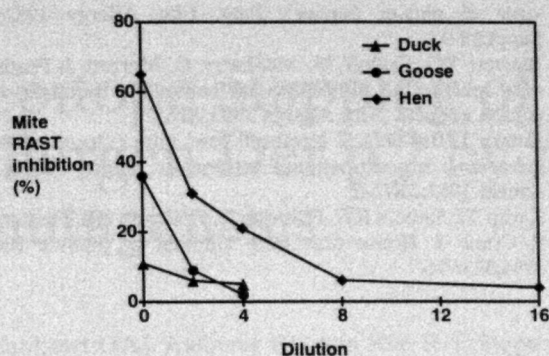


Fig. 4. Inhibition of mite RAST with unrefined feather extracts (duck and goose) and Soluprick hen feather SPT solution.

HDM extract. This may be due to real HDM allergy and be a sign of a favorable habitat for the mite in old feather pillows and down quilts. Linna et al. (16) have shown immunochemical cross-reactivity between a hen-feather extract and an HDM-allergen extract. It is possible, however, that most HDM SPT reactions were nothing but cross-reactions between Der p and bird mites, which are frequently found in unrefined feathers.

The paucity of positive RAST results to a feather mix, only three positives out of 177 atopic patients, was also a striking result. It is probable that only one of the three patients with elevated RAST values in feather multi-RAST (1.5 kU/l) was clinically allergic to feathers in spite of the fact that she also reacted to HDM. Another patient with a high feather mix RAST result (6.7 kU/l) was also allergic to hen's egg and apparently had the "bird-egg syndrome" (17, 18).

The allergen profile of feather extracts is not fully known. Allergens might consist of feather keratin and serum albumin (19, 20). The antigens involved in bird breeder's lung are contained in feather dust, including keratin particles coated with IgA (20), but also bird serum and feces (5). The feathers of cage birds, at least budgerigar and pigeon, contain allergens of *Pterolichus* mites, which seem to be the most important allergens in the feathers of these birds (21). In addition, the *Ornithonyssus sylvarium* mite living on fowl was related to allergic symptoms and occupational asthma (22). The present results suggest that mite allergens are responsible for positive SPTs in most cases, but that real feather allergy also exists, although it is extremely rare.

Kemp et al. showed that polyester-filled pillows contain significantly more total weight of Der p I allergen than feather-filled pillows (23). The down used in modern feather pillows and down quilts is carefully refined. Rough dry dust is removed first, after which the feathers are washed and dried. The

drying is done at 125°C. The high temperature also sterilizes the down.

In conclusion, SPT reactions to commercial feather-allergen products are fairly common but clinical allergy to feather proteins is much rarer than is usually thought. The allergens derived from unrefined feathers include various proteins, including those of bird serum, feces, and bird mites and their wastes. A positive SPT reaction to a feather preparation often means allergy to various mites, not to the feather itself. Feather products made of refined material seem to be safe for most SPT-positive patients.

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