

31445

Bird-Egg Syndrome

Cross-Reactivity between Bird Antigens and Egg-Yolk Livetins in IgE-Mediated Hypersensitivity¹

Michèle M. Mandallaz, Alain L. de Weck, Clemens A. Dahinden

Institute of Clinical Immunology, Bern University Hospital, Bern, Switzerland

Abstract. 87 adult patients from our allergy clinic were skin tested with budgerigar and canary feathers, hen's egg white and egg yolk and common inhalant allergens. Of 59 patients found to be atopic, 17 (29%) were concomitantly sensitized to bird dander and egg proteins, 10 of them being symptomatic to bird dander and/or egg exposure. All but 1 of the egg-symptomatic patients were exposed to pet birds. The patients with strong serological reactivity to bird antigens were also exclusively sensitized to egg proteins, in particular to livetins (water-soluble fractions of egg-yolk proteins). Extensive RAST-inhibition studies demonstrated identical patterns of cross-reactivity between bird dander and hen's egg proteins, livetins being the major cross-reacting antigens. This peculiar IgE-mediated allergy is designated as 'bird-egg syndrome'. It is suggested that egg intolerance in adults is mainly due to sensitization to egg-yolk livetins and can be provoked by inhalation of pet bird dander. Thus, it must be distinguished from the common egg-white allergy of atopic children. Our study further underlines the importance of respiratory sensitization in adult food allergy. On the other hand, exposure to cross-reacting antigens by ingestion might also influence the allergic manifestations to inhalant allergens.

Introduction

Hypersensitivity to hen's egg white is rather frequent in atopic individuals, especially in children, and has been extensively studied [1-9]. Whereas IgE-mediated hypersensitivity to egg-yolk proteins is seldom reported in the literature. The major egg-white allergens are known to be ovalbumin, ovomucoid and ovotransferrin, and IgE-class antibodies to egg white are usually found in patients with egg intolerance [10-12]. However, the antibody titers are not clearly correlated with the severity of the clinical manifestations [5-7]. The IgE-mediated reactions vary from urticaria and angioedema, flare-up of atopic dermatitis and gastrointestinal symptoms to asthma or even anaphylactic shock [2, 8]. These manifestations usually subside gradually throughout life and intolerance to egg or egg products is much less frequent in adults than in infancy. The ingestion of egg proteins seems to be the major route of sensitization, but occasional

reports on allergy to inhaled egg material have been published [13, 14, 32].

Food-allergic adult patients are often sensitized to pollens and such syndromes as concurrent IgE-mediated allergy to tree pollens and fruits [15,16] or to Compositae pollens and vegetables (parsley family) [17, 18] are now well recognized and thought to be due to antigen cross-reactivities. One of our patients, who started with asthma due to her budgerigar at the age of 42 and subsequently developed egg allergy, was exclusively sensitized against bird feathers, egg-white and egg-yolk proteins, and made us aware that a similar cross-reactivity might exist for hen's eggs and other avian antigens. Indeed IgG antibodies against egg-yolk proteins have been described in workers exposed to egg spray [13, 14, 30] and recent research on extrinsic allergic alveolitis (pigeon's breeder lung) demonstrated cross-reactivity of precipitating antibodies to bird antigens among several species [19, 20] and with the water-soluble egg-yolk proteins known as 'livetins' [21-23]. However, only 1 patient with asthma was recently reported to have parrot-specific IgE antibodies cross-reacting with crude egg-yolk extracts [24].

¹ This work was supported by the Swiss National Science Foundation, grant No. 3.278-0.85.

The present paper describes the results obtained in 59 atopic adults systematically skin tested with budgerigar and canary feathers, egg white, egg yolk and pure livetin extracts and all the common pneumo-allergens. We found that simultaneous allergy to bird antigens and egg proteins is rather common and, in 10 patients symptomatic to egg and/or bird feathers, serological investigations were performed. In all the patients with elevated specific IgE antibodies to budgerigar antigens, we could demonstrate serological cross-reactivity with egg proteins.

Our results suggest that, in adult patients with a predominant sensitization to bird and egg proteins, the major cross-reacting determinants are the livetins. The route of sensitization seems to be primarily respiratory in some patients, with ensuing food allergy to egg by cross-sensitization. On the contrary in other patients, sensitization by ingestion of egg proteins might precede the respiratory allergies elicited when a bird is introduced to the home. We propose to designate this particular cross-reactivity as 'bird-egg syndrome'.

Materials and Methods

Clinical Investigations

Skin tests were performed in 59 atopic and 28 nonatopic subjects in a standardized manner with 10–14 perennial inhalant antigens and 8 pollen antigens. A careful history was taken in particular for the presence of a bird at home and eventual symptoms after egg ingestion or contact with birds.

The skin tests included intradermal tests to perennial antigens (Bencard 0.5%): house dust, feathers, two different mould extracts and various animal hair extracts (sheep, horse, goat, camel, eventually cat, dog, guinea pig and rabbit according to the patient's exposure to these animals), scratch tests with *Dermatophagoides pteronyssinus* and *D. farinae* (Pharmacia 10,000 BU/ml) and prick tests to pollen antigens (Stallergènes) including a mixture of five grasses, Timothy pollen 1/20, rye 1/20, two groups of tree pollens, two groups of weeds and mugwort. In addition, intradermal tests to budgerigar and canary feathers (Bencard 0.2%) and to hen's egg white and egg yolk (Stallergènes 1/100) were performed in all patients. In 19 patients, purified livetins, prepared as below, were tested intradermally at several concentrations (0.0001, 0.001, 0.01, 0.1, 1 mg/ml) as well as ovalbumin (1 mg/ml; Sigma).

The livetins from hen's egg yolk were prepared as follows: using fresh unfertilized eggs, the egg yolk was carefully separated from egg white and rolled over an absorbant paper. The vitelline membrane was then opened with a needle and the egg yolk collected. The yolk was stirred with the same volume of 0.16 M NaCl and the yolk granules were removed by centrifugation at 20,000 g for 2 h at 4°C. The supernatant was separated into livetins and lipoproteins by ultracentrifugation as previously described [25, 26].

Serological Investigations

Routine RAST tests were performed with commercial antigen-coated paper disks and reagents (Pharmacia) following the procedure recommended by the manufacturer.

For ovalbumin and livetin RAST, ovalbumin (Sigma) or livetins, purified by ultracentrifugation as described above, were coupled covalently to paper disks: 300 mg CNBr-activated [27] paper disks (Whatman filter paper) were incubated with 15 mg livetins in 2 ml 0.5 M NaHCO₃ at pH 8.4 for 24 h at 4°C. The supernatant was aspirated and the disks were washed. The remaining active groups were blocked with ethanolamin (10 ml, 0.05 M for 2 h at room temperature). After several washes in NaHCO₃ (0.1 M, pH 9.5), Na acetate (0.1 M, pH 4) and NaCHO₃ (0.5 M, pH 8.4), the disks were stored at 4°C in 0.1 M phosphate buffer (pH 7.4) containing 0.3% bovine serum albumin, 0.01 M EDTA, 0.2% azide and 0.2% Tween 20.

RAST Inhibition Studies

Preliminary experiments indicated that patient 2 had such high IgE antibody titers against bird and egg proteins that they completely saturated the disks. Dilution of serum to 0.1 still resulted in RAST classes 3–4, comparable to the titers of undiluted serum of patient 1. Thus for all inhibition studies, the serum of patient 1 was used undiluted and that of patient 2 was diluted to 0.1. The following antigens were used in fluid phase: (a) egg white from fresh unfertilized hen's eggs in phosphate-buffered saline (PBS); (b) purified livetins in PBS, the protein contents of both preparations were estimated by using an extinction coefficient at 280 nm = 1 AU/cm for 1 mg/ml protein; (c) a crude water-soluble extract from budgerigar dander. The concentration is given by dry weight per milliliter, the extract contained less than 1% protein.

One volume of antigen solution at different concentrations or buffer alone was mixed with 4 vol of serum and left overnight at 4°C before performing RAST experiments. 50 µl of this mixture were added to each disk. The percent inhibition was calculated as follows:

$$\frac{\text{cpm (RAST serum + antigen)}}{\text{cpm (RAST serum + buffer)}} \times 100.$$

Controls showed that none of these extracts had any influence on RAST against unrelated antigens, i.e. grass pollen or house dust mites.

Results

Case histories are described for the patients found to be symptomatic to bird feathers and/or egg proteins.

Case Reports

Case 1. A 47-year-old female, who had never experienced allergic manifestations before the age of 42, is indeed very similar to the case reported by de Maat-Bleeker et al. [24]. After acquisition of a budgerigar, she developed allergic perennial rhinoconjunctivitis and asthma attacks while cleaning the bird's cage, rapidly asso-

Table I. Clinical findings in 49 atopic patients, without symptoms to eggs or bird antigens, systematically skin tested for common inhalant allergens and bird and egg proteins

Skin-test reactivity to bird and egg proteins	Number of patients	Patients with possible symptoms to birds ¹ %	Positive skin tests to			Patients exposed to birds %	Number of positive skin tests to 20 other antigens (median)	Total IgE (median)
			bird %	egg white %	egg yolk %			
Bird, positive								
Egg proteins, positive	7	40	60	100	85	40	10	433
Bird, positive								
Egg proteins, negative	12	8	60	0	0	30	6.5	458
Bird, negative								
Egg proteins, positive	10	20	0	70	70	30	10.5	342
Bird, negative								
Egg proteins, negative	20	0	0	0	0	0.5	5	118

¹ In some patients, the partial responsibility of bird antigens for perennial symptomatology cannot be completely excluded.

ciated with a strong intolerance to eggs evoked as abdominal pain and throat pruritus but no systemic manifestations. The patient also noted conjunctivitis and contact urticaria of the hands when manipulating raw eggs, especially the egg yolks. The skin tests were exclusively and strongly positive to bird feather, egg white, egg yolk and livetin extracts.

Case 2. A 24-year-old female was known as allergic to eggs throughout her entire life. Eating half-cooked eggs had always elicited immediate vomiting and Quincke edema of the buccal region without systemic symptoms. She acquired a budgerigar and within a few weeks experienced for the first time rhinoconjunctivitis and exercise-induced symptoms, namely asthma and generalized urticaria of noncholinergic type. These symptoms could not be attributed to any other allergen than bird feathers, since all other skin tests and serological investigations, except for hen's egg white, egg yolk and livetins, were negative and the symptoms subsided after removal of the bird from the house.

Case 3. A 30-year-old female, with symptomatic pollinosis and severe animal allergy since puberty, suffered from asthma when she came in contact with various animals such as cats, dogs, horses, guinea pigs and hamsters. The skin tests were strongly positive to animal dander, egg proteins and budgerigar extracts. She precisely remembered that after acquiring a budgerigar during adolescence, she experienced a severe intolerance to eggs during a few years which rapidly disappeared when the bird was given away. She had no respiratory symptoms at that time and had never possessed a bird since then.

Case 4. A male patient, aged 30, suffered since childhood from severe vomiting, diarrhea and urticaria when eating eggs. The skin tests to hen's egg white, egg yolk and livetins were strongly positive and he also reacted intensively to budgerigar extracts although he had never possessed or been in contact with pet birds. He also suffered for years from pollinosis and cat allergy and the skin tests reacted accordingly.

Case 5. A female patient, aged 20, had pollinosis since infancy and atopic dermatitis for 3 years. She kept 40 birds at home but never had any perennial respiratory symptoms. She had almost never eaten eggs because she disliked them, but could not remember any reaction to egg ingestion. Except for pollens and animal dander, the only strongly positive skin tests were to budgerigar feathers, hen's egg white, egg yolk and livetins. Although the history of egg intolerance was questionable, this patient is included here because of her intense exposure to birds and strong skin reactivity to egg proteins in the absence of conscious and voluntary egg exposure.

Case 6. A 44-year-old female was referred to the clinic for chronic urticaria and Quincke edema attacks for 1 year. She also had asthma, which disappeared as urticaria started, and egg intolerance characterized by gastralgias. The skin tests showed a strong reactivity to dog hair and bird feathers and a slight reactivity to hen's egg white. All other investigations were negative. The patient gave her budgerigar away and went through an egg-free diet which improved her symptoms.

Case 7. A 40-year-old female had suffered from pollinosis and asthma elicited by house dust and cats for more than 15 years. She kept canaries at home for 10 years without precisely related symptoms until a few weeks before consultation, when cleaning the bird's cage provoked several asthma attacks. Except for urticaria to strawberries, she had no food and particularly no egg intolerance. The skin tests were strongly positive to many inhalant allergens including canary feathers, and to commercial hen's egg-white and egg-yolk proteins.

Case 8. A 36-year-old female had symptoms of allergic perennial rhinitis and asthma for a few months and exclusively when she stayed at home. She had previously suffered from chronic rhinitis as a child but had never experienced intolerance to egg or egg products. She kept a dog, 2 cats and a bird at home. Except for a sensitization to grass pollens, the only positive skin tests were to canary

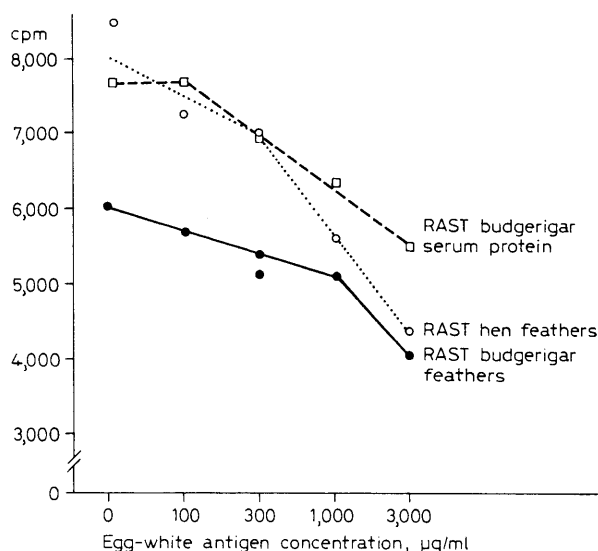


Fig. 1. RAST inhibition of high concentrations of fresh hen's egg white on RAST to various avian antigens in patient 1.

and budgerigar feathers, her bird's nest, hen's egg white and egg yolk.

Case 9. A female patient, aged 30, who was asymptomatic until 1986, had an asthma attack while cleaning the cage of her canary. The skin tests showed that she was sensitized to many animals, including birds, cats, horses and guinea pigs, but also very strongly to hen's egg white but not to egg yolk. She had always eaten eggs without problems and there was no evidence of atopy in the family.

Case 10. A 45-year-old female, who had no previous history of allergic manifestations, came to the clinic for the investigation of a chronic asthmatic cough and several urticarial outbreaks which developed a few months before consultation, clearly when the patient was staying at home. She had acquired a budgerigar a year before and the symptoms were attributed to the presence of this bird since they subsided when it was given away. She had no clinical intolerance to eggs. The skin tests were strongly positive to bird feathers and egg white but not to egg yolk.

In conclusion, all 10 patients symptomatic to bird feathers and/or egg proteins concomitantly reacted in skin tests to bird antigens as well as hen's egg-white and/or egg-yolk proteins to varying degrees. The 2 patients who were most severely symptomatic to both bird and eggs (patients 1 and 2) had the strongest skin reactivity to bird feathers (budgerigar and hen), hen's egg yolk and purified livetins, and were exclusively sensitized to these antigens. They also had strongly elevated RAST to all the bird antigens tested (budgerigar feathers, budgerigar dung, budgerigar serum proteins, hen's feathers, goose feathers, duck feathers), as well as to hen's egg white and livetins but not to ovalbumin. These findings suggested the possibility of a

cross-reactivity between hen's egg and other avian antigens.

Of the other 77 patients tested as described in methods, 49 were found to have IgE-mediated symptoms to various antigens other than bird and egg proteins. The findings of these 49 atopic patients are summarized in table I. The results are presented in 4 groups according to the skin reactivity to egg and bird proteins. Only 7 patients (14%) were sensitized in skin tests to both bird and egg proteins. Interestingly only 3 of these patients kept a bird in contrast to the 90% of bird-exposed patients in the symptomatic group. Of the 28 patients without reactivity to all common inhalant allergens, none was positive to hen's egg proteins, purified livetins or bird antigens.

Serological Investigations

Extensive serological investigations including RAST-inhibition tests were undertaken in the patients 1 and 2 with strongly positive RAST to bird antigens and hen's egg proteins. The RAST to hen's egg white, livetins and budgerigar feathers were elevated in both patients (class 3-4), and we performed RAST-inhibition tests with fresh egg white, budgerigar dung and livetins. Budgerigar dung extract was used to represent bird antigens in all RAST-inhibition tests, since we had previously demonstrated that all the bird antigens (budgerigar serum proteins, feathers and dung as well as duck, goose and hen feathers) could be identically inhibited by this extract.

In the first patient, the RAST to budgerigar feathers and budgerigar serum proteins could not be inhibited by ovalbumin (2 mg/ml), but surprisingly could be inhibited with a high concentration of hen's egg white (3 mg/ml). Repeated experiments showed that this inhibition was reproducible but of variable intensity (data not shown). However, within the same experiment, the amount of inhibition by high concentrations of hen's egg white was similar for different avian antigens (fig. 1).

These results suggested that the cross-reactive antigen(s) is present in variable but minor quantities in egg white. To study the nature of the cross-reacting antigen(s) further, we systematically investigated RAST inhibition by fresh hen's egg white, purified livetins and budgerigar dung towards commercial egg white and budgerigar feather RAST disks, as well as livetins covalently coupled to paper disks.

RAST inhibition by egg white at low concentrations of 0.5-60 µg/ml confirmed that budgerigar anti-

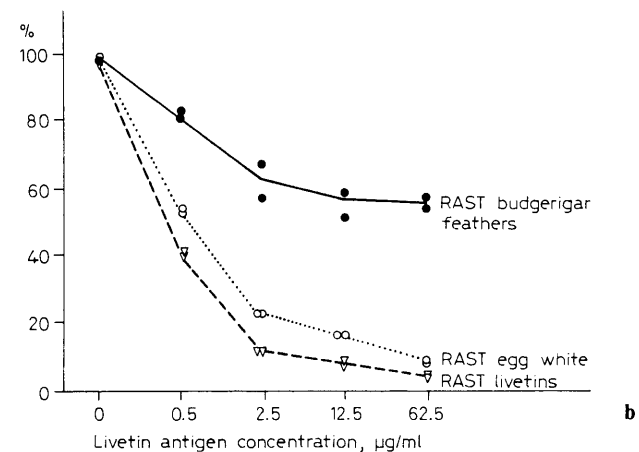
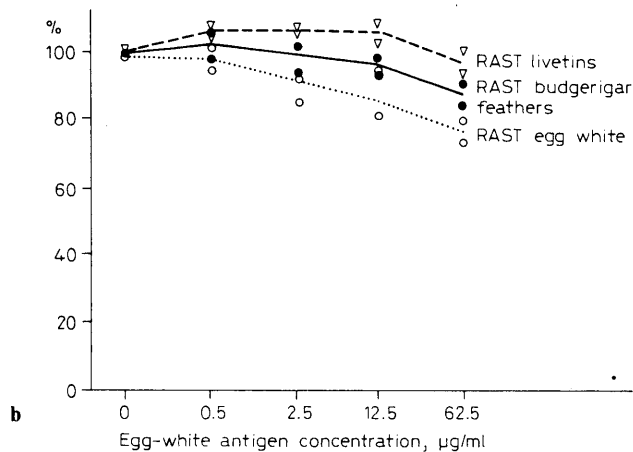
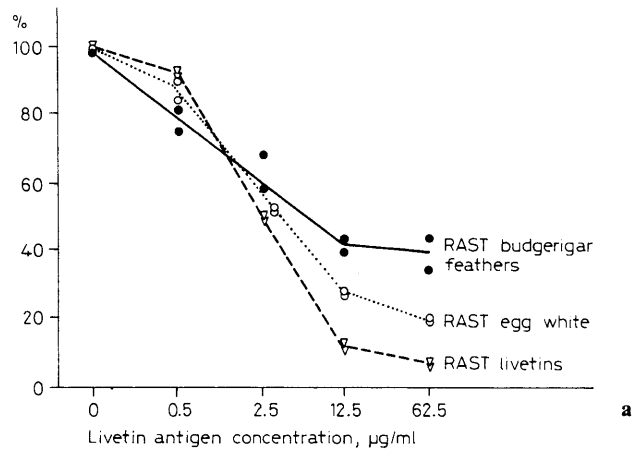
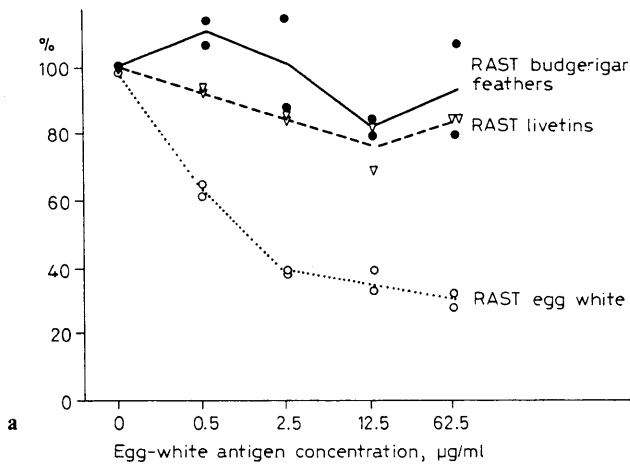


Fig. 2. RAST inhibition of hen's egg white at low concentrations on RAST to budgerigar feathers, egg white and livetins in patient 1 (a) and patient 2 (b).

Fig. 3. RAST inhibition of livetins on RAST to budgerigar feathers, egg white and livetins in patient 1 (a) and patient 2 (b).

gens could not be substantially inhibited. Also the RAST to livetins could not be inhibited with egg white, indicating that no substantial amount of cross-reacting egg-white antigen was present in our livetin preparation. Even RAST to egg white was only inhibited by 70 and 30%, respectively, in patients 1 and 2 (fig. 2), suggesting that other antigens might be present in the commercial egg-white RAST disks.

The RAST-inhibition tests with livetins showed that less than 60 µg/ml of livetins could inhibit the RAST to budgerigar feathers by 40–60% in both patients (fig. 3). Higher doses of livetins up to 1,000 µg/ml did not increase the inhibition (data not shown), indicating the presence of noncross-reacting antigens in bird extracts. Interestingly, the RAST to

egg white was inhibited with livetins by 80–90% in both patients, suggesting either contamination of the commercial egg-white RAST disks with egg yolk or the presence of a major antigen in egg white cross-reacting with a livetin component [11, 28, 29, 31]. As expected the RAST to livetin could be totally inhibited by livetins.

Finally, the inhibition tests with budgerigar dung antigen showed the same inhibition of RAST reactions to budgerigar feathers and livetin extracts (fig. 4), suggesting that all livetin antigens are present in bird dung extracts. Budgerigar dung could inhibit the RAST to egg white by 10% in the first patient and by about 50% in the second patient, confirming our interpretation of the results given in figures 1–3.

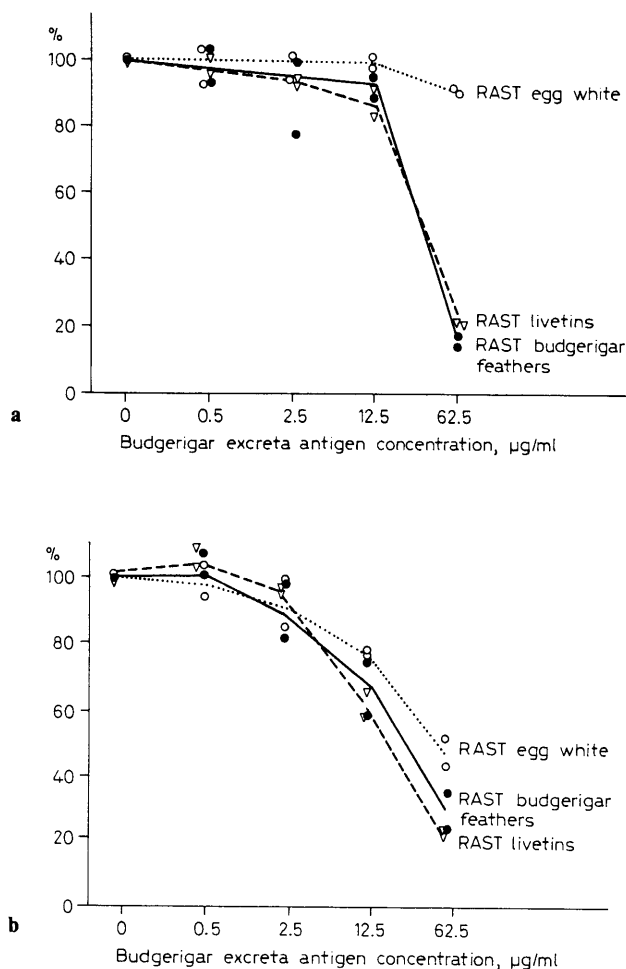


Fig. 4. RAST inhibition of budgerigar excreta antigen on RAST to egg white, budgerigar feathers and livetins in patient 1 (a) and patient 2 (b).

In summary, both patients were clinically and serologically exclusively sensitized to bird and egg proteins. The results of our investigations suggest that a major component of the antigenic reactivity in the serum of both patients is due to the livetins, which are responsible for the cross-reactivity between hen's egg yolk and bird proteins.

Discussion

The skin-test results in 59 atopic patients showed that the concomitant sensitization to bird and hen's egg proteins is in fact a rather common finding (29%).

All patients with clinical symptoms to one or the other antigen had at least some reactivity in skin tests to both antigens. The clinical findings in patients 1 and 3 indicate that the respiratory sensitization to budgerigar allergens might have been responsible for the egg intolerance. On the other hand, a previous sensitization to egg proteins could also predispose some patients to respiratory symptoms from birds. For example, patient 2, who was strongly allergic to eggs experienced respiratory symptoms immediately after acquiring a bird. In this patient, there is even a possibility that the egg allergy started with a sensitization to egg white in infancy and turned during adult life to a predominant allergy to egg yolk after exposure to a bird.

All patients symptomatic to eggs but 1 were exposed to birds and were all strongly sensitized in skin tests to hen's egg-white as well as egg-yolk proteins. Patient 4 who was severely allergic to egg proteins and sensitized in skin tests to egg white and egg yolk was also strongly sensitized to bird feathers although he had never been exposed to a pet bird. In this patient, a predominant, albeit weak, serological reactivity was found to egg white and also to a minor extent to budgerigar antigens and livetins. As a matter of fact, the predominant sensitization to egg-yolk proteins could partially explain the discrepancy between the antibody titers to egg white and the severity of symptoms in some adult patients symptomatic to eggs [5, 7].

Even in the 5 patients with asthma anamnestically due to pet bird dander but with no or doubtful symptoms to eggs, we found a positive skin reactivity to bird dander and egg proteins. This might represent a subclinical sensitization to certain egg antigens. Interestingly none of these patients had positive RAST tests to bird or egg antigens and therefore the antigens responsible for the symptoms cannot be definitely identified.

The 2 patients who were serologically positive to bird proteins were also clinically symptomatic to bird and egg antigens. In RAST tests they both reacted equally to the different bird antigens tested and to livetins. The pattern of RAST-inhibition experiments was almost identical in both patients with a total inhibition of livetins by budgerigar excreta and a partial inhibition of bird antigens by livetins. These results demonstrate that major cross-reacting antigen(s) are present in egg-yolk livetins. It also suggests that the IgE antibodies in these patients recognize very con-

served 'archaic' epitopes or proteins which are present in dander and serum of different avian species as well as in hen's egg-yolk livetins.

The reactivity to egg white is more difficult to interpret. In contrast to livetin RAST which were always strongly positive, there was a considerable variability in RAST results to egg white (class 1-4) with different batches of commercial egg-white RAST disks (data not shown). Also the positive RAST to egg white were inhibited by livetins. Both patients were negative to ovalbumin, a major egg-white protein. Nevertheless some cross-reacting antigens (for example ovotransferrin) might also be present in egg white [11, 29, 31].

Further studies should identify the nature of the cross-reacting antigen(s) in livetins. Preliminary immunoblotting experiments show an identical antigen pattern in both patients, with the presence of a major antigen in livetins not present in egg white. More extensive serological investigations are necessary to determine whether this pattern is the rule in patients with positive RAST to bird feathers and its prevalence. However, seropositivity to bird dander is rather rarely found even in patients with unambiguous respiratory symptoms to bird exposure (i.e. patients 6-10). In order to explain this, one might speculate that the cross-reacting IgE antibodies are cleared from the circulation by livetin proteins passing the intestinal barrier, especially in patients with low budgerigar-specific IgE antibodies and no recognized egg intolerance. Even the occurrence of oral desensitization towards cross-reacting antigens by chronic ingestion of eggs cannot be excluded.

In a survey of our sera collection, all sera positive to budgerigar feathers were also strongly positive to livetins, variably positive to egg white and negative to ovalbumin [Dahinden and Mandallaz, unpublished]. This would further document the very high prevalence of the 'bird-egg syndrome' in patients seropositive to bird antigens, which is caused by a sensitization to livetins. The clinical implication of this observation remains to be determined. In particular, it is not known whether it is necessary to recommend an egg-free diet for these patients in addition to avoiding exposure to bird dander.

Acknowledgments

We thank Mrs J. Grob and Mrs P. Winkler for their excellent cooperation and technical assistance.

References

- 1 Langeland, T.: Allergy to hen's egg white in atopic dermatitis. *Acta dermat.-vener., Stokh.* 114: 109-112 (1985).
- 2 Langeland, T.: A clinical and immunological study of allergy to hen's egg white. I. A clinical study of egg allergy. *Clin. Allergy* 13: 371-382 (1983).
- 3 Langeland, T.: A clinical and immunological study of allergy to hen's egg white. IV. Specific IgE-antibodies to individual allergens in hen's egg white related to clinical and immunological parameters in egg-allergic patients. *Allergy* 38: 493-500 (1983).
- 4 Husby, S.; Schultz Larsen, F.; Ahlstedt, S.; Svehag, S.-E.: Humoral immunity of dietary antigens in atopic dermatitis. II. Analysis of IgE and IgG subclass antibodies. *Allergy* 41: 386-391 (1986).
- 5 Atherton, D.J.; Sewell, M.; Soothill, J.F.; Wells, R.S.: A double-blind controlled cross-over trial of an antigen avoidance diet in atopic eczema. *Lancet* i: 401-403 (1978).
- 6 Atherton, D.J.: Allergy and atopic eczema. II. *Clin. exp. Dermatol.* 6: 317-325 (1981).
- 7 Shakib, F.; Brown, H.M.; Stanworth, D.R.: Relevance of milk- and egg-specific IgG4 in atopic eczema. *Int. Archs Allergy appl. Immun.* 75: 107-112 (1984).
- 8 Special Symposium: Significance of food hypersensitivity in children with atopic dermatitis. *Pediat. Dermatol.* 3: 161-174 (1986).
- 9 Anet, J.; Back, J.F.; Baker, R.S.; Barnett, D.; Burley, R.W.; Howden, M.E.H.: Allergens in the white and yolk of hen's egg. A study of IgE binding by egg proteins. *Int. Archs Allergy appl. Immun.* 77: 364-371 (1985).
- 10 Langeland, T.; Harbitz, O.: A clinical and immunological study of allergy to hen's egg white. V. Purification and identification of a major allergen (antigen 22) in hen's egg white. *Allergy* 38: 131-139 (1983).
- 11 Langeland, T.: A clinical and immunological study of allergy to hen's egg white. VI. Occurrence of proteins cross-reacting with allergens in hen's egg white as studied in egg white from turkey, duck, goose, sea gull and in hen egg yolk, and hen and chicken sera and flesh. *Allergy* 38: 399-412 (1983).
- 12 Rowntree, S.; Cogswell, J.J.; Platts-Mills, T.A.E.; Mitchell, E.B.: Development of IgE and IgG antibodies to food and inhalant allergens in children at risk of allergic disease. *Archs Dis. Childh.* 60: 727-735 (1985).
- 13 Edwards, J.H.; McConnochie, K.; Trotman, D.M.; Collins, G.; Saunders, M.J.; Latham, S.M.: Allergy to inhaled egg material. *Clin. Allergy* 13: 427-432 (1983).
- 14 Edwards, J.H.; McConnochie, K.; Davies, B.H.: Skin-test reactivity to egg protein exposure by inhalation compared with ingestion. *Clin. Allergy* 15: 147-150 (1985).
- 15 Dreborg, S.; Foucard, T.: Allergy to apple, carrot and potato in children with birch pollen allergy. *Allergy* 38: 167-172 (1983).
- 16 Halmepuro, L.; Vuontela, K.; Kalimo, K.; Björkstén, F.: Cross-reactivity of IgE antibodies with allergens in birch pollen, fruits and vegetables. *Int. Archs Allergy appl. Immun.* 74: 235-240 (1984).
- 17 Hannuksela, M.; Lahti, A.: Immediate reactions to fruits and vegetables. *Contact Dermatitis* 3: 79-84 (1977).
- 18 Wüthrich, B.; Dietschi, R.: Das «Sellerie-Karotten-Beifuss-Gewürz-Syndrom»: Hauttest- und RAST-Ergebnisse. *Schweiz. med. Wschr.* 115: 358-364 (1985).

- 19 Sennekamp, J.; Lange, G.; Nerger, K.; Berdel, D.; Meier-Sydow, J.: Human antibodies against antigens of the sparrow, blackbird, weaver finch, canary, budgerigar, pigeon and hen using the indirect immunofluorescent technique. *Clin. Allergy* 11: 375-384 (1981).
- 20 Faux, J.A.; Wells, I.D.; Pepys, J.: Specificity of avian serum proteins in tests against the sera of bird fanciers. *Clin. Allergy* 1: 159-170 (1971).
- 21 Berrens, L.; Verschuren, M.; Van Dijk, A.G.; Guikers, C.L.H.: Antibodies against hen's egg proteins in pigeon breeder's disease. *Clin. Allergy* 16: 355-363 (1986).
- 22 Williams, J.: Serum proteins and the livetins of hen's egg yolk. *Biochem. J.* 83: 346-355 (1962).
- 23 Cook, W.H.: Composition and properties of the proteins and lipoproteins of egg yolk; in Food science and technology. Proceedings of the 1st International Congress, pp. 259-265 (Gordon & Breach, New York 1962).
- 24 de Maat-Bleeker, F.; Van Dijk, A.J.; Berrens, L.: Allergy to egg yolk possibly induced by sensitization to bird serum antigens. *Ann. Allergy* 54: 245-248 (1985).
- 25 Burley, R.W.; Vadehra, D.V.: Chromatographic separation of the soluble proteins of hen's egg yolk: an analytical and preparative study. *Analyt. Biochem.* 94: 53-59 (1979).
- 26 Burley, R.W.; Cook, W.H.: Isolation and composition of avian egg yolk granules and their constituents alpha- and beta-lipovitellins. *Can. J. Biochem. Physiol.* 39: 1295-1307 (1961).
- 27 Lee, W.J.; Heiner, D.C.: Preparation of rabbit anti-IgE for use in radioimmunoassays of total IgE and specific IgE antibodies. *J. immunol. Methods* 20: 185-200 (1978).
- 28 McIndoe, W.M.; Culbert, J.: The plasma albumins and other livetin proteins in egg yolk of the domestic fowl (*Gallus domesticus*). *Int. J. Biochem.* 10: 659-663 (1979).
- 29 Hui, S.F.; Common, R.H.: Studies on the livetins of egg yolk. III. Heterogeneity and immunoelectrophoretic behavior of beta-livetin. *Can. J. Biochem.* 44: 1357-1364 (1966).
- 30 Berrens, L.; Edwards, J.H.: Antibodies to bird serum proteins in confectionery workers exposed to egg spray. *Clin. Allergy* 17: 405-408 (1987).
- 31 Walsh, B.J.; Elliott, C.; Baker, R.S.; Barnett, D.; Burley, R.W.; Hill, D.J.; Howden, M.E.H.: Allergenic cross-reactivity of egg-white and egg-yolk proteins: an in vitro study. *Int. Archs Allergy appl. Immun.* 84: 228-232 (1987).
- 32 Bernstein, D.I.; Smith, A.B.; Moller, D.R.; Gallagher, J.D.; Tar-Ching, A.; London, M.; Kopp, S.; Carson, G.: Clinical and immunological studies among egg-processing workers with occupational asthma. *J. Allergy clin. Immunol.* 80: 791-797 (1987).

Received: February 16, 1988

Correspondence to: Dr. Clemens A. Dahinden
Institut für klinische Immunologie
Inselspital
CH-3010 Bern (Switzerland)