

Egg yolk α -livetin (chicken serum albumin) is a cross-reactive allergen in the bird-egg syndrome

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Abstract

Thirty-one patients with clinical history of egg allergy, bird allergy, or bird and egg allergy were investigated with the use of the immunoblot technique to compare IgE-binding components in bird feather and egg yolk and white extracts. Patients were classified into three groups according to clinical history, skin prick test results, and RAST results. Patients in group I were sensitized to bird feathers and egg yolk, patients in group II to egg white, and patients in group III to bird feather but not to eggs. Patients with bird-egg syndrome were mainly female adults, whereas egg white allergy was mainly observed in children without any obvious sex predisposition. IgE from patients with bird-egg syndrome recognized a 70 kd protein in egg yolk (chicken serum albumin = α -livetin) and some major allergens in bird feather extract (70, 95, and 200 kd). Preincubation of pooled sera from patients with bird-egg syndrome with budgerigar or hen feather extract and egg yolk extract, respectively, led to complete blocking of IgE binding to allergens in egg yolk and bird feather extract. On the other hand, IgE from patients with egg white allergy did not react with allergens in egg yolk and bird feather extract, despite strong IgE binding to egg white allergens. Patients in group III displayed no reactivity to bird feather or egg allergens. Our results demonstrate common epitopes of budgerigar and hen feather and egg yolk α -livetin. Therefore we assume that α -livetin (chicken serum albumin) leads to a cross-sensitization and consequently to the "bird-egg syndrome." (J ALLERGY CLIN IMMUNOL 1994;93:932-42.)

MW Molecular weight

SDS-PAGE Sodium dodecyl sulphate–polyacrylamide gel electrophoresis

Key words: [Allergens](#), [bird-egg syndrome](#), [egg yolk](#), [cross-reactivity](#), [IgE antibodies](#), [chicken serum albumin](#)

A relationship between particular inhalational type I allergies and food hypersensitivities is becoming more evident. In the past, research concentrated on pollen allergies associated with fruit and vegetable intolerance.¹⁻⁴ More recently, cross-reactions between bird allergens and egg yolk antigens have been described.⁵⁻¹²

TABLE I. Patient clinical history

Patient	Age (yr)	Sex	<u>Symptoms after</u>		<u>Onset of symptoms to</u>		<u>Allergic reaction to</u>		Bird at home	Bird removed
			Egg ingestion	Bird contact	Egg ingestion	Bird contact	Eggs	Birds		
1	42	F	LS, conj, dysp	Dysp, asth, conj	1/2 yr ago	5 yr ago	Immed.	Immed.		Parrot, 3 yr ago
2	29	F	Urt	Rhin, asth, dysp	Days ago	1 mo ago	Immed.	Immed.	>10 yr, budgerigar	
3	47	F	None	None					Since 4 yr, budgerigar	
4	59	F	LS, burning throat	Dysp, asth, rhin, conj	20 yr ago		Immed.	Delayed	>5 yr, budgerigar, canary	
5	49	F	Urt, vomiting	Rhin	3 mo ago	1/2 yr ago	Immed.	Immed.	2 yr, 2 budgerigars	
6	51	F	Prur, urt, asth, ana	Dysp, asth, fever	10 yr ago	25 yr ago	Immed.	Immed.	1968-1969, budgerigar	1969
7	46	F	Burning throat	Rhin, conj	8 yr ago	10 yr	Immed.	Immed.	8 yr, budgerigar	
8	58	F	Emesis	Asth, dysp	4 yr ago	4 yr	Immed.	Immed.	9 yr, ara	
9	42	F	Throat edema	Asth, dysp	1/2 yr	2 yr ago	8-hr delay	Immed.	7 yr, budgerigar	
10	43	M	None	Bronch		Weeks ago		Immed.	1 yr, budgerigar	
11	43	M	None	Asth, rhin, conj		Many yr ago		Immed.	1 yr, budgerigar	
12	71	M	Dysp	Dysp, asth	>20 yr ago	5 yr ago	Immed.	Immed.	6 yr, budgerigar	
13	16	F	Face	Asth	6 yr ago	Recently	Immed.	Immed.	10 yr, parrot	

			edema						
			Derm, prur, cramps, diarrhea						
A	37	F		20 yr ago	Immed.				
B	24	M	Derm, LS, rhin	Many yr ago	Immed.		Since yr, budgerigar		
C	4	M	Derm	Since birth	Delayed				
D	1	M	Derm	1/2 yr ago	Delayed				
E	3	M	Derm, ana	Since birth	Immed.				
F	11	F	Derm, perioral swelling	4 yr ago	Immed.		Many yr, canary		
G	10	F	Derm, oral prur	Early childhood	Immed.				
H	39	F	Derm, LS	Childhood	Immed.				
I	6	F	Derm, prur	5 1/2 yr ago	Immed.		Since birth, budgerigar		
J	21	F	Derm	6 yr ago	Immed.				
K	21	M	Derm	Since birth	Immed.				
L	7	M	Derm	4 yr ago	Delayed				
M	52	F	Derm	51 yr ago	Delayed				
I	30	F	None	Cough, rhin	1 yr ago	Immed.	1 yr, budgerigar	10 days ago	
II	51	F	None	Rhin, conj	10 yr ago	Immed.	15 yr, budgerigar		
III	40	F	None	Rhin, conj, dysp	1 yr ago	Immed.	>2 yr, budgerigar		
IV	17	F	None	Dysp	Many yr ago	Immed.	6 yr, parrot		
V	33	F	None	Rhin, dysp, conj	15 yr ago	Immed.	12 yr ago, budgerigar		

LS, Lip swelling; *conj*, conjunctivitis; *dysp*, dyspnea; *prur*, pruritis; *urt*, urticaria; *asth*, asthma; *ana*, anaphylaxis; *derm*, dermatitis; *rhin*, rhinitis.

Hypersensitivity to hen's egg white is rather frequent in atopic individuals, especially in children with atopic dermatitis. [13-15](#) Egg protein sensitivity usually appears during the first and second years of life, abates later on, and may even disappear. Various allergens have been identified in hen's egg white and egg yolk, [14, 16-19](#) but most publications have dealt with egg white allergens because of its relevance to nutritive allergies in infancy. The occurrence of egg protein allergy in adults is much less frequent, but if it appears, it seems to be induced or facilitated by a previous inhalational sensitization to avian antigens. [5-12](#)

De Maat-Bleeker et al.⁵ first described the case of a 65-year-old female patient who complained of allergic rhinitis and asthma in the presence of a parrot. At the same time, she experienced severe symptoms (urticarial rash, angioedema) after ingestion of eggs. RAST inhibition experiments revealed IgE cross-reactivity between antigens present in parrot serum and hen's egg yolk antigens. A similar case was reported by Hoffman and Guenther.⁶ More recent data revealed that IgE antibodies cross-reacted between livetins, an egg yolk protein fraction, and bird feather antigens, thus leading to a bird-egg syndrome.^{7, 9, 11} However, in all of these studies relatively few patients were investigated, and most of the studies were single case reports. In the present study 31 patients with egg allergy, bird allergy, or bird and egg allergy were investigated to compare IgE-binding components in bird feather and egg yolk extracts and to further characterize the cross-reacting allergens.

Methods

Sera

Sera from 10 female and 3 male patients with egg yolk allergy and bird feather hypersensitivity who ranged in age from 16 to 71 years (median age, 46 years) (test group I) were selected according to positive case history, positive skin prick test results, and positive RAST results (>2.0) to budgerigar and hen feather extract and egg yolk and egg white extracts. Sera from 13 patients with egg white protein allergy without any sensitization to bird feather proteins (7 female and 6 male subjects) who ranged in age from 1 to 52 years (median age, 11 years) served as group II. Sera from patients with bird feather allergy but without sensitization to egg proteins according to the above cited criteria ($n = 5$; 5 female patients, with age ranging from 17 to 51 years; median age, 33 years) served as group III. ■Table I shows the patients' histories and the symptoms experienced after either egg ingestion or bird contact, onset of symptoms to both offending allergen sources, immediate or delayed reaction, duration of bird keeping at home, and bird species. We also attempted to delineate the sequence of appearance of symptoms. In 9 of 13 patients in group I, the onset of symptoms of allergy to birds preceded the clinical reaction to egg ingestion. In three patients the reaction to egg ingestion preceded reactions to bird contact, whereas in one patient no clinical symptom has been described so far despite repeated positive skin prick test reactions and high specific IgE levels to egg and bird feather antigens.

In group II none of the patients experienced allergy symptoms as a result of bird contact. A bronchial challenge test with bird feather extracts was not performed. Only 3 of 13 patients also had birds at home. In group III all five patients had a bird at home and experienced mild respiratory symptoms as a result of bird contact or inhalation of allergen-contaminated air near the cages.

■Table II shows the serologic data of the patients with positive skin prick test reactivity to a variety of allergens; specific IgE reactivity to egg white, egg yolk, bird feather, and other allergens is given as the RAST class and total IgE is expressed in kilounits per liter.

TABLE II. Patient serologic data

Patient	Age (yr)	Sex	Positive skin prick test reactivity	Specific IgE (RAST units)					Others	Total IgE (kU/L)
				f1	f75	f83	e78	e85		
1	42	F	Goose, duck, hen, parrot, egg, egg white, egg yolk	3,4	3,9	3,2	3,8	4,5	e5 2	812
2	29	F	Egg, egg yolk	3,1	3,5	2,7	4	3,9		770
3	47	F	Egg, egg yolk, birch, alder, hazel, mite	3	3,8	3,6	4	5	d1 4.0, t3 3.5, g3 2.3	>1000
4	59	F	Egg, egg yolk	3,6	3,6	3	4	4,2	e1 2.5	>1000

5	49	F		1,3	2,1	1,9	3,4	2,4	f4 3.7, f5 4.0	280
6	51	F	Egg, egg white, egg yolk, guinea pig, goose, duck	3,4	4	3,6	4	5		770
7	46	F	Egg white, cat, guinea pig	3,2	2,4	2	3,2	2,4		>1000
8	58	F	Egg yolk, goose, pig, mite, budgerigar	2,1	3,3	2,7	2,4	3,6		509
9	42	F	Egg, egg white, egg yolk	2,2	3,3	2,7	2,2	4	e1 2.0	318
10	43	M	Egg, egg yolk, hamster	3,2	3,5	3,1	4	5	e84 2.6	>1000
11	43	M	Birch, rye, grass pollen, cat	3,1	3	2,3	3,8	3,4	g3 5, w6 2.2, t3 2	>1000
12	71	M	Egg, egg yolk, goose, hen, mite	2,3	3,8	3,1	2,7	5		210
13	16	F	Rabbit, cat, guinea pig, horse, egg, dog, grass, birch, nuts	3,7	3,7	2,2	2,5	3,6	d1 3.2	>1000
A	37	F	Mite, cow, cat, rabbit, egg, egg white, egg yolk, milk	4	2,6	2,1	0	1,1	d1 3.9, t3 3.6, f2 3.9	>1000
B	24	M	Egg, egg white, rabbit, cat, guinea pig, horse, cow, mite	3,6	1,8	0	0	1,1	d1 5	>1000
C	4	M	Wheat, soya, egg white, egg, milk	4,1	3,3	3,1	1,5	4,4	f2 3.9, f4 3.7, f14 2.9	>1000
D	1	M	Dog, rabbit, cat	5	3,2	2,4	1,2	2,5	e1 4, e5 3.8, f2 3.3	>1000
E	3	M	Birch, cat	5	2,1	0	0	0	f2 2.4, f14 1.5, f×1 2.1	>1000
F	11	F	Hazelnut, peanut, egg, egg white	5	2,4	0	0	1	t3 5, f14 2.8, f×1 5	900
G	10	F	Mite, dog, cat, horse	3,3	2,5	1,1	0	2,2	e1 5, e5 5, f2 1.1	>1000
H	39	F	Mite, egg, egg white, egg yolk, shrimp, horse	3,7	1,3	3,1	0	1,5	d1 3.5	>1000
I	6	F	Dog, rabbit, cat, guinea pig, horse, cow, egg, egg white + yolk	3,5	0	0	0	0	d1 2.1	165
J	21	F	Egg, egg white	3,3	0	0	0	0		>1000
K	21	M	Grass, rye, wheat, dog, cat, egg white, birch, alder, hazel	3,6	2,2	1,1	0	2,5	g3 3, d1 4, e1 3	480
L	7	M	Egg white, egg, egg yolk	4	3	0	0	2,2	f4 3.4, d1 2.4	>1000
M	52	F	Egg, egg white, egg yolk, milk, grass, mugwort, ragweed, mite, cat, dog, rabbit	5	3,8	2,5	0	4,5	d1 3.8	>1000
I	30	F	Birch	0	0	ND	2,4	ND		255
II	51	F	Grass, rye, goose, duck, hen, mugwort	2,3	2,3	2,4	2,6	2,2	f4 3.3, f5 3.3, g3 5	736
III	40	F	Birch, alder, hazel	2,1	2,1	2,4	2,4	2,2	e1 2.4, t2 3.7, t3 5, d1 3	386
IV	17	F	Parrot. duck. goose. hen.	0	0	ND	2	ND		806

budgerigar

V	33	F	Grass, wheat, rye, cat	0	0	ND	2,2	ND	g3 5	173
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Specific RAST extract abbreviations: *f1*, egg white; *f75*, egg yolk; *f83*, chicken meat; *e78*, budgerigar feather; *e85*, hen feather; *e5*, dog; *d1*, house dust mite; *t3*, birch pollen; *g3*, grass pollen; *e1*, cat; *f4*, wheat; *f5*, rye; *e84*, hamster; *w6*, mugwort; *f2*, cow's milk; *f14*, soya; *f×1*, nut mix; *t2*, alder.
ND, Not done.

Sera collected from 10 individuals with negative case history for any type I allergy, negative skin prick test and negative RAST results to bird proteins and egg proteins served as the control group. All sera were stored at -20°C . Before use, sera were dissolved 1:10 in buffer.²⁰

Protein extracts

Soluble hen feather and budgerigar feather extracts were purchased from Miles Inc., Hollister-Stier Div. (West Haven, Conn.). Egg yolk and egg white were purchased from Allergon AB (Engelholm, Sweden) and extracted according to the method of Ipsen and Löwenstein²¹ with slight modifications: freeze-dried raw material was extracted in 10 mmol/L potassium dihydrogen phosphate (pH 7.0) containing 2% (wt/vol) suspended solid polyvinylpolypyrrolidone, 2 mmol/L of ethylenediaminetetraacetic acid disodium salt, 10 mmol/L of sodium diethyldithiocarbamate, and 3 mmol/L sodium azide under continuous shaking for 24 hours at 4°C . Particles were removed by centrifugation (40,000g for 1 hour at room temperature). The supernatant was extensively (72 hours, 4°C) dialyzed against 10 mmol/L of potassium dihydrogen phosphate (pH 7.0) containing 3 mmol/L of sodium azide, lyophilized, and stored at -20°C .

Before use for electrophoresis, extracts were dissolved in distilled water and diluted in concentrated Laemmli sample buffer.²²

The protein concentrations of the protein preparations were measured according to the method of Bradford²³ with bovine serum albumin as standard (Protein Assay, Bio-Rad, Munich, Germany).

All skin prick tests were performed with commercially available aqueous extracts from ALK (Copenhagen, Denmark). Allergen-coated RAST sheets for all allergens were purchased from Pharmacia (Uppsala, Sweden). The extracts were not identical for the applied experiments, and this might explain discrepancies between RAST and prick test results. In our study the prick test results were less sensitive when compared with the clinical symptoms and the specific RAST results. For immunoblotting and inhibition experiments, the allergenic protein extracts of egg yolk and egg white (Allergon AB) and budgerigar and hen feather (Miles Inc., Hollister-Stier Div.) were used. In previously comparative sodium dodecylsulfate–polyacrylamide gel electrophoresis (SDS-PAGE) runs Hollister-Stier products turned out to be superior to ALK products with respect to the number and clearness of protein bands.

SDS-PAGE and immunoblotting

SDS-PAGE was carried out as described previously.²⁰ Protein concentrations of egg yolk, egg white, budgerigar feather, and hen feather extracts were 30 μg , 50 μg , 30 μg , and 30 μg per minigel, respectively. The separated proteins were transferred onto nitrocellulose (pore size = 0.45 μm ; Schleicher & Schuell, Dassel, Germany) at 300 mA for 60 minutes at 4°C .²⁴ IgE blots were performed as described previously.²⁰

The SDS-PAGE experiments were also repeated under nonreducing conditions. The results obtained were identical to denaturing conditions.

Inhibition experiments

Sera from 13 patients (group I) with IgE-binding to the major allergens of egg yolk (70 kd) and bird feather (70, 95, and > 200 kd) were pooled, diluted 1:10 in buffer (50 mmol/L of sodium phosphate, 0.5 [vol/vol] of Tween 20, 0.5% [wt/vol] of bovine serum albumin, and 0.05% [wt/vol] of sodium azide, pH 7.5) and preincubated with 0.225, 0.028, and 0.0017 mg/ml egg yolk extract, with 0.1, 0.012, and 0.0008 mg/ml

budgerigar or hen feather extract, respectively and 0.46 mg/ml egg white extract, under continuous shaking overnight at 4° C. Thereafter, nitrocellulose strips coated with budgerigar and hen feather, egg yolk and egg white extracts, respectively, were incubated with these preincubated sera, and bound IgE was detected as described previously. Additionally, pooled sera of group I were preincubated with 1.0, 0.5, 0.2, 0.1, 0.05, 0.01 mg/ml chicken serum albumin (Sigma Chemical Co., St. Louis, Mo.) before subsequent testing on egg yolk– and budgerigar–coated strips.

Results

IgE immunoblots

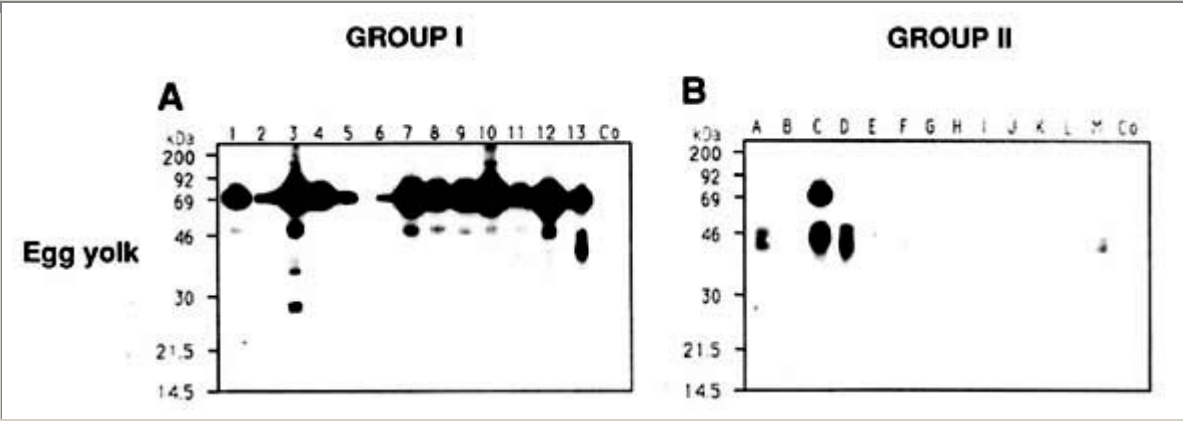
IgE reactivity of sera from individuals with bird feather allergy and egg yolk hypersensitivity (group I)

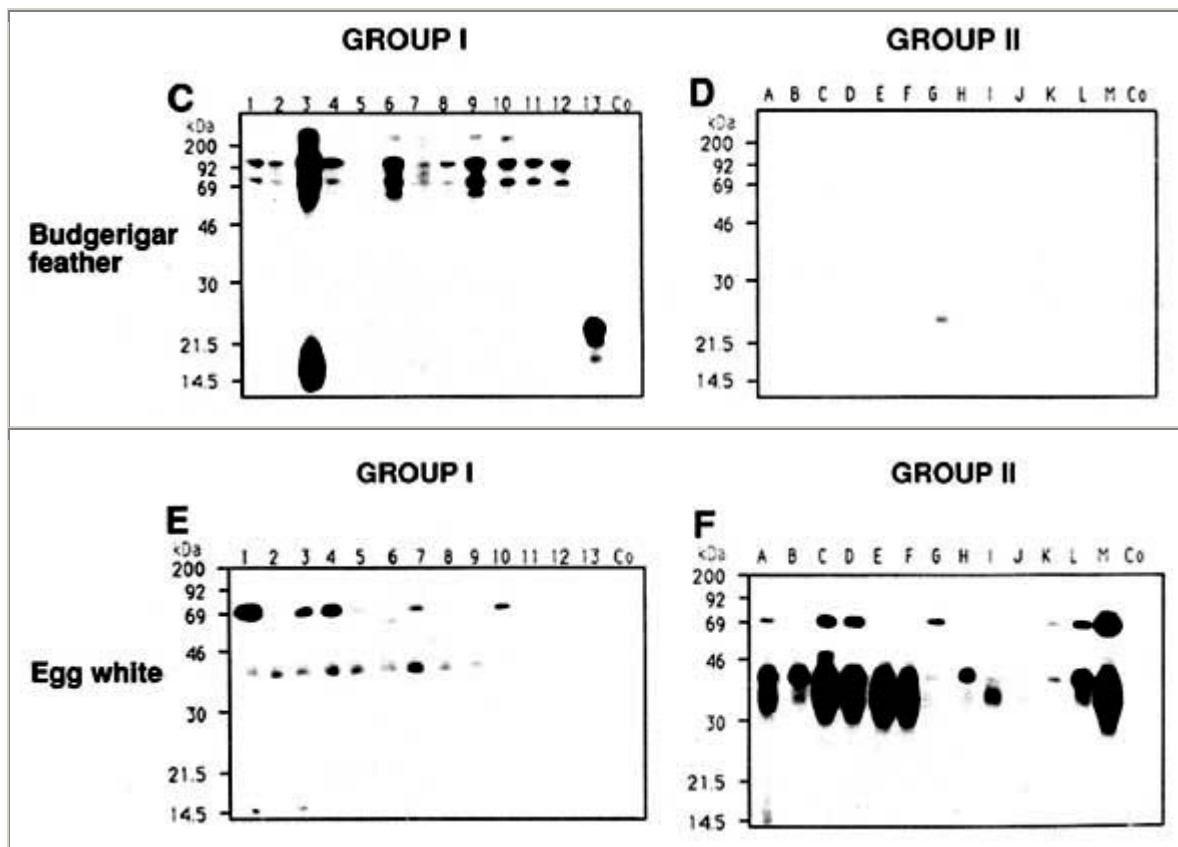
With egg yolk extract, all 13 patients (100%) demonstrated IgE binding to a 70 kd protein, and four patients (31%) reacted exclusively with this protein (patients 2, 4, 5, and 6; ■Fig. 1, A). Sera from eight patients (61%) recognized a 50 kd protein, sera from five patients recognized a 40 kd protein, and sera from four patients reacted with other minor allergens (26, 42, 150, and > 200 kd) (■Fig. 1, A).

Almost all patient sera that reacted with the 70 kd protein of egg yolk (12 of 13, 92%) demonstrated IgE binding to proteins of budgerigar feather extract in the molecular weight (MW) region of 70, 95, and 200 kd (■Fig. 1, C). With regard to hen feather extract, eight of 13 patients reacted with proteins of the same MW as shown for the budgerigar extract. Discrepancies between IgE binding to budgerigar and hen feather extracts were possibly due to lower IgE-binding affinity to hen proteins in patients primarily sensitized by budgerigar at home. When exposing the blots for longer periods (up to 2 weeks) by autoradiography, previously unreactive sera would reveal positive antibody binding.

With egg white extract, 11 of 13 patients (84%) showed weak IgE binding to proteins with MWs of 40 to 45 and 70 kd (■Fig. 1, E).

FIG. 1. IgE immunoblots with sera from 13 patients with bird-egg syndrome (group I) and 13 patients with egg white allergy (group II) on egg yolk–coated strips (A,B), budgerigar feather–coated strips (C,D), and egg white extract–coated strips (E,F).





IgE reactivity of sera from patients with egg white allergy (group II).

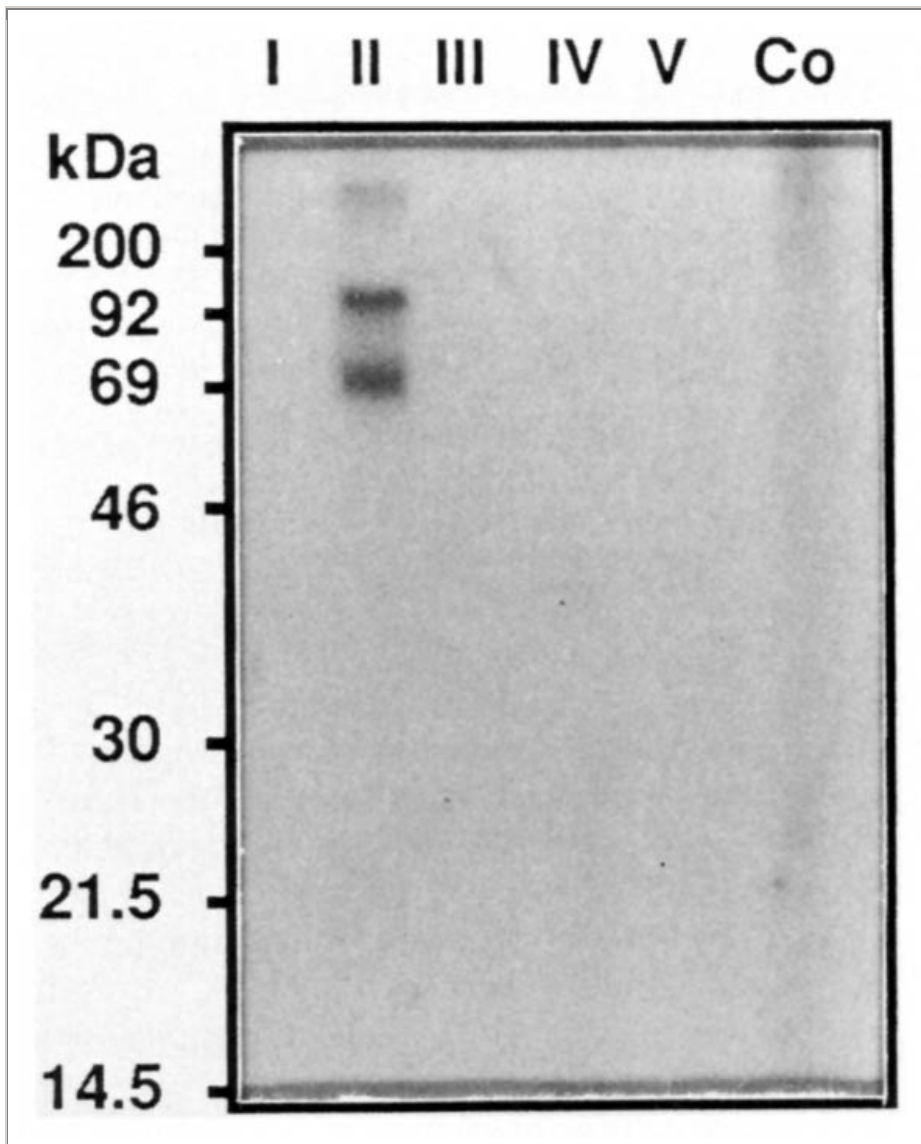
With egg white extract, all patients' IgE (13 of 13) reacted with a 40 to 45 kd protein, sera from 10 of 13 (76%) with a 35 kd protein, and sera from 8 of 13 (61%) with a 70 kd protein (■Fig. 1, F). Only patient C showed, in addition, IgE binding to a 70 kd protein on egg yolk extract (■Fig. 1, B). IgE from five of 13 patients bound to minor allergens on the egg yolk extract (50 and 45 kd, ■Fig. 1, B). No IgE binding to allergens in budgerigar feather extract was observed (■Fig. 1, D).

IgE reactivity of patients with bird feather allergy without egg yolk allergy (group III).

IgE from patients I and IV reacted with budgerigar and hen feather proteins with MWs of 60, 70, 95 kd and 17 and 75 kd, respectively (■Fig. 2). From these immunoblot results one could assume that in fact three of the five patients in group III were not allergic to bird feathers. The serologic data illustrate the very low level of specific IgE antibodies to bird feathers. Additionally, autoradiography for longer times (up to 2 weeks) would reveal positive antibody binding. Sera from two of five patients showed IgE binding to egg yolk proteins with MWs of 70 kd (patient II) and 95 kd (patient IV). All five patients demonstrated weak IgE binding to egg white proteins (45 and 70 kd).

The sera from the control group contained no IgE antibodies specific for bird feather and egg extracts as determined by immunoblotting analyses (■Fig. 1, A-F).

FIG. 2. IgE immunoblots with sera from five patients having symptoms caused by bird contact (group III) on budgerigar extract-coated strips.



Inhibition experiments

Preincubation of group I serum pool (see Methods section) with a concentration of 0.1 mg/ml hen and budgerigar feather extract was sufficient to strongly reduce IgE binding to egg yolk allergens (■Fig. 3). IgE binding to the major allergen of egg yolk (70 kd), as well as to minor allergens with MWs of 40 and 50 kd, was completely blocked. Preincubation of group I serum pool with concentration of 0.225 mg/ml egg yolk extract abolished IgE binding to major allergens of hen and budgerigar feather extracts. Preincubation of group I serum pool with egg white extract with subsequent testing on feather or egg yolk extract-coated strips resulted in no inhibition of IgE binding (■Fig. 4). Preincubation of group I serum pool with bird feather or egg yolk extract and subsequent testing with bird feather- or egg yolk extract-coated strips led to complete blocking of IgE binding, respectively (■Fig. 4).

FIG. 3. Inhibition experiment. Sera from 13 patients in group I were pooled, and inhibition was carried out by preincubation with 0.1, 0.012, 0.0008, and 0 mg/ml budgerigar feather extract (*I, II, III, IV*); 0.225 mg/ml egg yolk extract (*EY*); and 0.46 mg/ml egg white extract (*EW*).

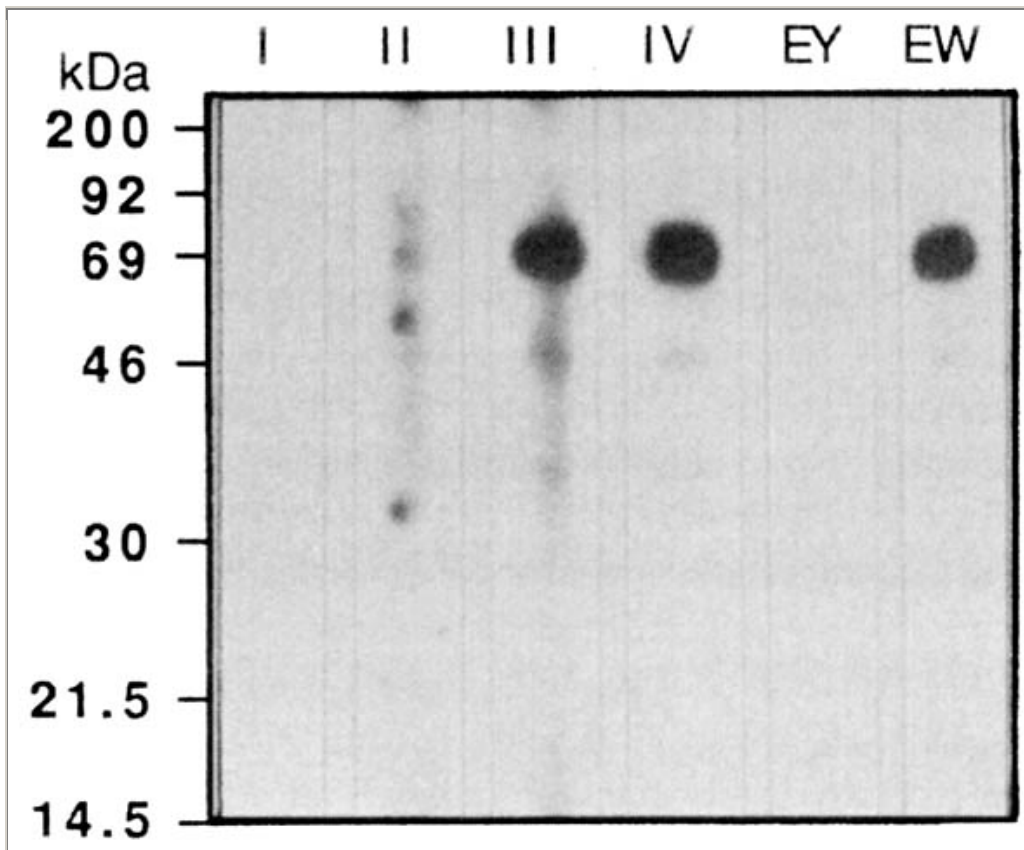
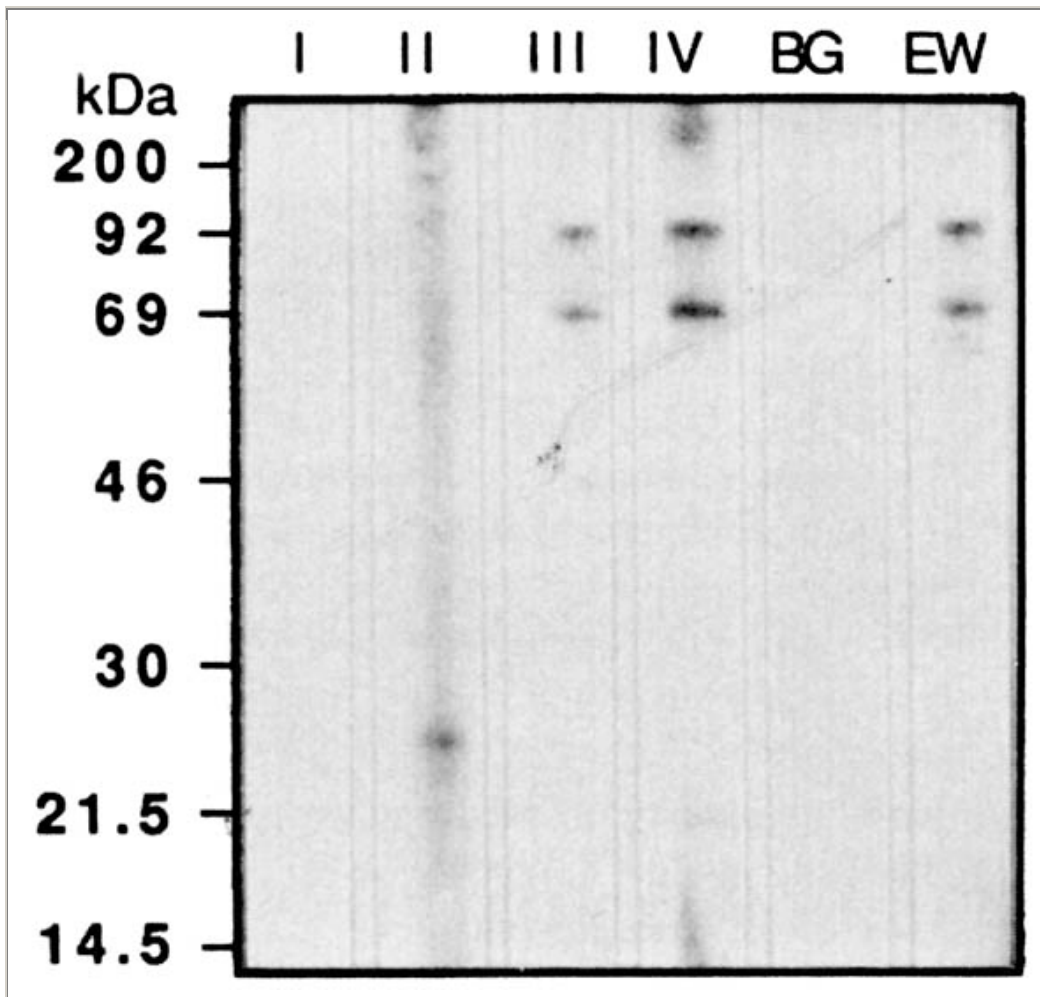
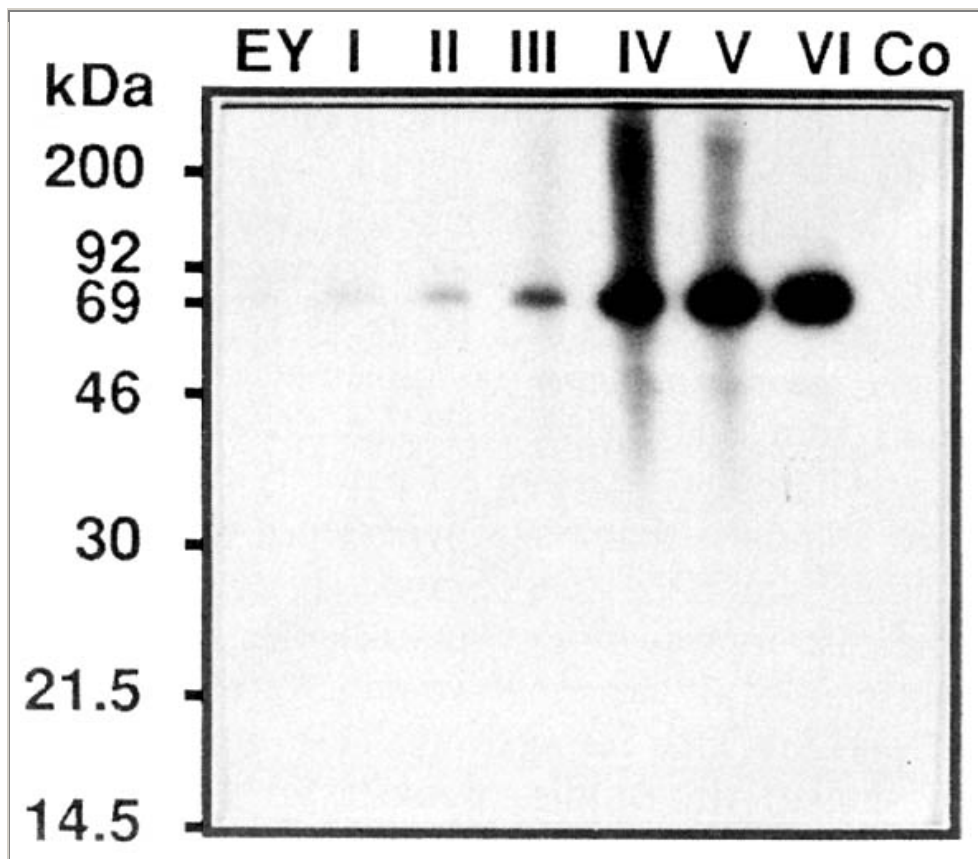


FIG. 4. Inhibition experiment. Sera from 13 patients in group I were pooled, and inhibition was carried out by preincubation with 0.255, 0.028, 0.0017, and 0 mg/ml egg yolk extract (*I, II, III, IV*); 0.1 mg/ml budgerigar feather extract (*BG*); and 0.46 mg/ml egg white extract (*EW*).



Furthermore, preincubation of sera of group I with increasing concentrations of chicken serum albumin led to increasing inhibition of IgE binding to the 70 kd protein in egg yolk (Fig. 5), as well as to the 70, 95, and 200 kd proteins in budgerigar and hen feather extracts. These results provide evidence for the identity of chicken serum albumin and α -livetini.

FIG. 5. Inhibition experiment. Sera from 13 patients in group I were pooled, and inhibition was carried out by preincubation with 1.0, 0.5, 0.2, 0.1, 0.05, and 0 mg/ml chicken serum albumin (I, II, III, IV, V, VI) and 0.01 mg/ml egg yolk (EY).



Discussion

TOP

Recently, several publications have described the occurrence of egg allergy combined with hypersensitivity to bird antigens in adults.⁵⁻¹² It was shown that egg yolk proteins, and in particular livetins, were responsible for this cross-reactivity of specific IgE antibodies. This observation led to the term “bird-egg syndrome.”^{7, 8, 10, 11}

The purpose of the present investigation was to compare IgE-binding components in bird feather and egg yolk extracts to further characterize cross-reacting allergens. With the use of the immunoblot technique, serum IgE from 13 patients with bird-egg syndrome (allergic to egg yolk and bird feather) (group I), 13 patients with egg white allergy (group II), and five patients with bird feather allergy without nutritive hypersensitivity to egg proteins (group III) were investigated with respect to their capacity to react with allergens in egg yolk, egg white, bird feather extracts, and chicken serum albumin.

Our observations revealed that: (1) patients with bird-egg syndrome are mainly female adults, whereas egg white allergy most commonly occurs in children, without any sex predisposition; (2) IgE from patients with bird-egg syndrome binds to a 70 kd protein in egg yolk and some major allergens in bird feather extract (70, 95, and 200 kd); (3) IgE antibodies from patients with bird-egg syndrome detect cross-reactive proteins in egg yolk and bird feather extract as mentioned previously; (4) these cross-reactive proteins seem to be identical proteins, namely chicken serum albumin (i.e., egg yolk α -livetins); and (5) the IgE pattern of patients with bird-egg syndrome differs from that of children with egg white allergy.

The relatively large number of patients allowed us to analyze in more detail the composition of the bird-egg syndrome population. Age analysis of the patient groups (Table III) revealed a median age of 46 years (range, 16 to 71 years) in the bird-egg syndrome group I and a median age of 11 years (range, 1 to 52 years) in the egg white-allergic group II. Group III patients (those with bird allergy without egg hypersensitivity) had a median age of 33 years (range, 17 to 51 years). The case reports by De Maat-Bleeker et al.⁵ and Hoffman et al.⁶ describe two patients with ages of 65 and 31 years, respectively. This observation is consistent with studies published by other authors.^{7, 11} Analysis of variance and the Kruskal-Wallis H test reveals significance for this correlation ($p < 0.05$) in our patient groups. We would therefore

suggest that the occurrence of a bird-egg syndrome is typical in adulthood. Additionally, we deduced from our data a predominance of the female sex in the bird-egg syndrome group. This finding is again in accordance with the results of the other publications concerning this topic, although they are only case reports. The results of group III are quite inconclusive. The age and sex predominance would wane in the bird-egg syndrome group. On the other hand, the immunoblot results reveal IgE reactivity with egg yolk proteins (70, 95 kd) only in two of five patients and weak reactivity with egg white and bird feather proteins in one of five patients. These serologic and immunoblot data leave the tendency to develop a bird-egg syndrome open. A thorough clinical observation and repeated immunoblot testing with bird feather and egg yolk extracts might predict the outcome for these patients.

TABLE III. Classification of patient groups according to clinical history, RAST results, and skin prick test responses to budgerigar and hen feather extract and egg yolk and white extracts

	Bird-egg syndrome (group I)	Egg white allergy without bird allergy (group II)	Bird allergy without egg allergy (group III)
Number	13	13	5
Female	10	7	5
Male	3	6	0
		Age (yr)	
Median	46	11	33
Range	16-71	1-52	17-51

Our immunoblot experiments indicate that cross-reactivity of a 70 kd protein in egg yolk and some major allergens in bird feather extract (70, 95, and 200 kd) is associated with the bird-egg syndrome. Blocking of IgE antibodies directed against the 70 kd egg yolk protein by preincubation with budgerigar and hen feather extracts showed that all bird-egg syndrome-related allergens are present in bird feather extract. Sera of group I also lost their capacity to bind to bird feather antigens when preincubated with egg yolk. We conclude that all bird-egg syndrome-related antigens are present in egg yolk, as well as in budgerigar and hen feather extracts. This finding was only partially shown by previous investigations in which RAST and RAST inhibition techniques were used.

What is the nature of this antigen? Mandallaz et al.⁷ described a partial inhibition of budgerigar RAST after blocking with livetins. Pauli et al.²⁵ were able to show by means of immunoblot experiments in one case that the patient had IgE antibodies to the livetin fraction of egg yolk and to hen serum and hen feather proteins with an MW of 66 kd. Nevertheless, no inhibition studies were performed to demonstrate the cross-reactivity of these IgE antibodies. Our results clearly demonstrate the presence of at least common epitopes of bird feather and egg yolk α -livetins. α -Livetin, a protein isolated and characterized in hen's egg yolk and identified as hen serum albumin, is a protein with an MW of 70 kd.^{15, 26} Burley and Vadehra²⁶ clearly described 5 fractions in egg yolk by chromatographic separation of soluble egg yolk proteins. The α -livetin fraction had an MW of 70 kd and clearly differed from β -livetin (42 kd), γ -livetin (150 kd), δ -livetin (200 kd), and apovitellin II (20 kd). Williams¹⁵ found that α -livetin and chicken serum albumin produced single symmetric peaks in the ultracentrifuge. In starch-gel electrophoresis at a pH of 8.6, α -livetin and chicken serum albumin produced sharp bands, which had identical mobilities, and trypsin digests produced indistinguishable peptide patterns when subjected to electrophoresis at a pH of 6.4 and chromatography. In addition, arginine, tyrosine, and histidine content of the cleaved peptides was identical in α -livetin and chicken serum albumin digests. In our study all patients of group I (13 of 13) reacted with α -livetin, and this IgE-binding could be blocked by preincubation with chicken serum albumin. Additionally, a dose-dependent blocking to budgerigar and hen feather extracts was observed. Therefore we assume that chicken serum albumin represents the antigenic protein present in egg yolk (α -livetin) and bird feather and bird serum, thus representing the cross-reactive protein responsible for the bird-egg syndrome. Inhalation of bird serum, feather, or dropping material might trigger the development of sensitization to serum albumin. Therefore chicken serum albumin, processed by

the respiratory tract antigen-presenting cells, would be the offending antigen in this particular cross-reactivity model.

Patient C (group II) represents the only exception to the homogeneous IgE immunoblot pattern of group III (■ Fig. 1, B). Although the clinical findings of the patient who was 4 years of age were confined to egg white allergy, the immunoblot results revealed strong IgE binding to egg yolk α -livetins (70 kd). Bird feather hypersensitivity was not observed. Nevertheless, this patient's IgE displayed strong reactivity with hen feather proteins (70, 95, 200 kd) but no reactivity with budgerigar feather proteins. This observation and the discrepancy between immunoblot results of group I with budgerigar and hen feather extracts indicates that some isoforms of α -livetins or chicken serum albumin do exist. Protein sequencing of α -livetins and chicken serum albumin of different species would provide a deeper insight into this hypothesis.

The question of whether or not egg-free and hen-free diet for patients sensitized to bird feathers and avoidance of exposure to birds in patients with egg allergy should be recommended has been discussed.^{7, 8} Reactivity of IgE with α -livetins or chicken serum albumin might identify patients in whom bird-egg syndrome may develop.

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