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**ALLERGY TO EGG YOLK POSSIBLY INDUCED BY
SENSITIZATION TO BIRD SERUM ANTIGENS**

F. DE MAAT-BLEEKER, MD; A. G. VAN DIJK, MSc; and
L. BERRENS, PhD, FACA

Hypersensitivity to ingested hen's egg yolk is described in a 65-year-old female patient. The patient's symptoms started in adult life and coincided with the acquisition of a parrot as a household pet. The bird's presence caused complaints of allergic rhinitis, while the ingestion of eggs caused urticaria and angioedema. Analysis of sequential blood serum samples revealed high levels of IgE antibodies to egg yolk and to various bird sera, but no precipitins. RAST-inhibition experiments indicated that the primary sensitization may have been to antigens from the parrot.

ALLERGY TO HEN EGG is observed quite often in atopic individuals, but especially in children. The first symptoms usually become apparent in early childhood and tend to subside gradually, although they may persist into adult life. In 1912, Schloss¹ described a 14-month-old boy who developed urticaria and facial oedema after ingesting egg. A variety of other symptoms associated with egg hypersensitivity has since been described. Besides urticaria and angioedema, symptoms of gastrointestinal upset, respiratory distress, and even anaphylactic shock have been reported. In children with atopic dermatitis, the ingestion of egg may cause a flare-up of the eczema; elimination of egg from the diet has in these cases been shown to have a beneficial effect.² There is a general consensus that the major allergens reside in the egg white fraction, ie, mainly ovomucoid, conalbumin, and ovalbumin.³⁻⁵

Studies on the natural history of egg hypersensitivity^{6,7} have shown that children outgrow this particular food allergy, presumably due to maturation of the IgA-associated immune system in the gut.⁸ Ford and Taylor⁶ recently reported that the symptoms in the resolved group are either cutaneous or gastrointestinal, whereas the subjects with persistent egg allergy mostly suffered from angioedema and respiratory distress.

The present paper describes the exceptional case of egg allergy in a 65-year-old lady, whose symptoms only became apparent after the age of 50, and who had never

before had any symptoms of hypersensitivity to food. Apart from occasional episodes of mild recurrent bronchitis when a young woman, she had never experienced manifest allergic disease. The major antigens in this case did not reside in the egg white, but in the yolk. It became apparent that the onset of this peculiar allergy coincided with the acquisition of a parrot as a house pet. The presence of this bird caused complaints of allergic rhinitis and asthma, which resolved when the animal was removed. She became aware, however, of similar respiratory symptoms when visiting friends who kept parakeets, and of food allergy symptoms when eating hen eggs. Our clinical and serologic investigations strongly support the view that the food allergy to egg yolk had been induced by respiratory sensitization to bird serum proteins.

Materials and Methods

Blood samples were obtained by venous puncture. After clotting in glass, the sera were stored at -70°C until use. Using fresh hen eggs, the white was separated from the yolk; crude egg white antigens were then prepared by extraction with phosphate-saline buffer, followed by dialysis and lyophilization. This material also served as a source for the preparation of ovomucoid and ovalbumin, as described by Bleumink and Young.³ The egg yolk was suspended in acetone with vigorous stirring; the insoluble residue was separated, dried in air, and extracted with phosphate-saline buffer. After centrifugation, the aqueous extract was dialysed and lyophilized; the yolk extract probably contained most of the livetin and phosvitin protein fractions.⁹ Antigens

From the departments of Clinical and Experimental Allergy, University Hospital, Utrecht, the Netherlands.

from bird droppings were obtained commercially. All these antigens were coupled to paper discs with cyanogen bromide by the method of Ceska et al.¹⁰ The radioactive anti-IgE reagent for RAST was purchased from Pharmacia Diagnostics AB, Uppsala, Sweden. Results of RAST are expressed in percentage of activity bound to the allergen discs relative to the total radioactivity added per tube.

Results

Case History

In October 1982 a then 65-year-old Dutch female patient was examined at the request of the internal resident. She had severe symptoms of egg allergy, which became prominent in 1967 when, after consuming a rather soft-boiled egg, she experienced a widespread urticarial rash, with oedema of the face and glottis. There had been no episodes of gastrointestinal or respiratory upset, nor of anaphylaxis. Since then, she noted similar symptoms after consuming food containing even a small amount of egg, ie, cake, cookies, egg nog, etc, which caused itching and swelling of the lips persisting for hours. Skin contact, for example with mayonnaise or uncooked chicken meat, caused immediate urticaria and a severe burning sensation when taken by mouth. She could eat fried chicken without untoward effects. The patient could not recall any gross intestinal disturbances in the past. After the finding of many positive RAST results to bird antigens (see "Serologic Investigations"), careful questioning revealed that the onset of the above symptoms coincided with the acquisition of a parrot in the home. The bird's presence clearly caused allergic respiratory symptoms, ie, nasal discharge, irritation of the conjunctivae and wheezing, which subsided after the bird had been removed. But she noticed symptoms whenever exposed to birds as house pets and whenever consuming eggs or egg products.

The family history revealed no evidence of atopic disease; however, the patient had a fairly extensive medical history of internal and cardiac problems. She had a history of an appendectomy in 1930 and of a cholecystectomy in 1949. She was admitted to the internal ward in 1965 because of suspected hyperthyroidism. A diagnosis of Graves' disease was made on clinical and biochemical evidence of hyperthyroidism, an enlarged thyroid gland, and slight exophthalmos. After 2 years of unsuccessful treatment with propylthiouracil, a subtotal thyroidectomy was performed in 1967 (the year egg sensitivity appeared). Three months after the operation, hypothyroidism developed with severe obesity, cold intolerance and hoarseness, which was treated with desiccated thyroid hormone and levothyroxine, respectively. Despite satisfactory laboratory parameters, the patient remained obese. Hypertension developed in 1980, which was treated successively with mefruside, α -methyl dopa, and propranolol. In May

1983, the patient developed a large inferior myocardial infarction; she expired by heart failure in March 1984.

Skin tests

All clinical skin testing was done with the patient's approval and informed consent. Intracutaneous tests with a series of common inhalant allergens produced positive Type I reactions only with commercial house dust and human dander extracts. Prick tests with commercial extracts of unspecified concentration of both whole egg and egg yolk evoked strongly positive immediate reactions; prick tests with egg white extracts produced marginal results. Lyophilized extracts of parrot excreta, at 1 mg/mL gave positive intracutaneous test reactions, whereas the response to intradermal tests with ovomucoid (0.1 mg/mL), ovalbumin (1 mg/mL), β -lactoglobulin (10 mg/mL), and lyophilized egg yolk extract (1 μ g/mL) remained negative. In view of the patient's heart condition, further skin tests at this stage appeared unwarranted.

Serologic Investigations

Subjects with hypersensitivity pneumonitis (of which there was no clinical evidence in our patient) due to avian antigen exposure usually have IgG-class precipitating antibodies in the blood serum.^{11,12} Investigation of sequential serum samples in our case produced negative results by double immunodiffusion in agar for precipitating antibody to a variety of antigens, including egg yolk, egg white, serum proteins from chickens, parrots, budgerigars, canaries and pigeons, or antigens in the excreta of parrots, chickens or pigeons. Complement fixation tests with soluble antigens from bird excreta were negative.¹³ Likewise, a highly sensitive complement consumption assay for IgG-type anti-egg white antibody gave negative results.¹⁴ The levels of the acute phase protein CRP were below the limit of detection.

Levels of total IgE, determined by PRIST, were above normal, though not excessively high (Table 1). Quite fascinating, however, was the detection of very high levels of specific IgE antibodies by RAST against the blood serum proteins of chicken, parrot, budgerigar,

Table 1. Serial Results of PRIST for Total IgE and RAST for IgE Antibodies to Avian Products in the Propositus' Blood Serum*

Source material	April 12, 1983	Date June 6, 1983	Dec 16, 1983
Egg white	N.D.	0	0
Egg yolk	28	26	9
Chicken serum	35	30	19
Parrot serum	38	36	28
Budgerigar serum	27	24	26
Canary serum	24	21	26
Pigeon serum	34	30	14
Pigeon droppings	0	0	0
Total IgE	660	400	330

* Total IgE (PRIST) in kU/L. RAST-results in percentage binding of added radioactivity to the antigen-coated discs in a direct assay; N.D. = Not Done.

canary, and pigeon (Table 1). It was also extraordinary to find strong IgE antibody titers against soluble proteins from the yolk, but not the white, of hen eggs. The IgE antibody levels decreased considerably after the patient had been warned to avoid egg-containing food-stuffs.

Although antigenic cross-reactivities among avian serum proteins have often been reported,^{11,15} immunologic similarity between such sera and chicken egg yolk is less well documented. In order to study this aspect of possible cross-sensitization in our patient, a series of RAST-inhibition experiments was performed. In one set of experiments, the patient's serum (50 μ L) was preincubated with increasing dilutions of parrot serum prior to evaluation of IgE binding to egg yolk protein-coated discs by RAST. In a second series, the patient's serum was preincubated with various concentrations of egg yolk protein, whereupon residual IgE was measured by RAST with paper discs coupled to parrot serum. The results, shown collectively in Fig 1, clearly demonstrate that the strongest inhibition occurred by parrot serum of IgE binding to egg yolk antigens. With 0.5 μ g of total parrot serum protein, complete inhibition of IgE binding to egg yolk was observed (at a dilution of 5×10^{-3} , see Fig 1). Inhibition in the reverse situation was much less pronounced, because at yolk protein concentrations ≥ 0.5 μ g, the maximum inhibition attained a value of only 40% (Fig 1). This indicates that the IgE binding cross-reacting antigen occurs in much lower concentration in egg yolk than in parrot serum, or that egg yolk proteins do not contain all the sensitizing determinants. These results therefore suggest that the primary sensitization in our patient occurred by way of the inhaled parrot antigens, and that the ensuing food- and contact allergy to egg yolk was due to cross-sensitization.

Discussion

To the best of our knowledge, this is the first patient in whom IgE antibodies to egg yolk, but not to egg

white, and to avian serum proteins has been described. The case is also different from cases of egg allergy in children described by Dannaeus and Iganäs,¹⁶ where IgE and IgG antibodies against egg white proteins paralleled in most cases. No precipitating antibody was detectable in our patient against any of the investigated antigens. In consequence, the situation is also essentially different from patients with bird fancier's lung and coeliac disease described by Faux et al,¹⁷ who had precipitating IgG- but not IgE-antibodies against avian serum proteins and an antigen in hen egg yolk. Precipitating antibodies against the yolk proteins have also been reported by Edwards et al¹⁸ in professional workers exposed to egg spray, but these patients had no specific IgE antibodies.

It is known that the excreta of birds contain serum proteins^{11,12} and that there is extensive cross-antigenicity among the sera of various avian species, particularly among the albumins and β -glycoproteins.¹⁵ These serum proteins are also known to occur among the water soluble components (so-called 'livetins') in egg-yolk.⁹ Sensitization to bird serum proteins by inhalation of dry avian excreta, in terms of IgG antibody production, has been well-documented.^{11,12} The case of our patient illustrates that IgE-mediated egg allergy may be induced by the inhalation of proteins associated primarily with (fragments of) avian serum components in the dust of the excreta. Obviously, this peculiar kind of induced food allergy in a patient of advanced age is totally different from the more common egg allergies in children.^{6,7}

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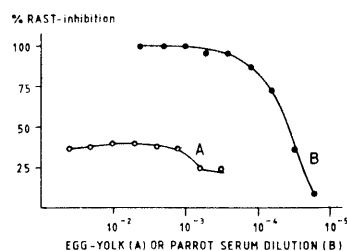


Figure 1. Inhibition of IgE binding (in RAST) to discs coupled with parrot serum from the serum of the propositus incubated with 50 μ L egg yolk dilutions (A, stock solution contained 10 mg of soluble protein/mL), and of IgE binding to discs coupled with egg yolk proteins from the patient's serum incubated with 50 μ L diluted whole parrot serum (B, undiluted protein concentration 50 mg/mL).

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Requests for reprints should be addressed to:
Prof. Dr. L. Berrens
Department of Experimental Allergy
University Hospital
Catharijnesingel 101
3511 GV Utrecht
The Netherlands

"Each generation should rather live its own life and leave behind it a definite achievement for the race as a whole. It would be a better heritage for the child than merely to have brought him into being and clothed and fed and given him what we call an education. An education is of very little worth unless the individual can use it and add to it the meaning of his own life."

Pearl S. Buck
At Home in the World

THE WISDOM OF WINSTON CHURCHILL

"History with its flickering lamp stumbles along the trail of the past, trying to reconstruct its scenes, to revive its echoes, and kindle with pale gleams the passion of former days. . . . As the great scroll of history unrolls, many complicated incidents occur which it is difficult to introduce effectively into the pattern of the likes and dislikes of the epoch in which we live. The human story does not always unfold like a mathematical calculation on the principle that two and two make four. Sometimes in life they make five or minus three; and sometimes the blackboard topples down in the middle of the sum and leaves the class in disorder and the pedagogue with a black eye."

Winston Churchill