

Allergy to inhaled egg material

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Summary

The use of a spray system to coat meat rolls with egg solution resulted in the development of asthmatic type symptoms in eight of thirteen workers exposed to the spray. Symptoms were severe in five workers, less severe in two, and one worker experienced vague symptoms. Even though precipitins were present in nine of the workers there were no pyrexial episodes nor influenza-like symptoms occurring some hours after inhaling the egg material to suggest extrinsic allergic alveolitis.

All sera with precipitins reacted against an antigen in egg yolk, two sera only to this antigen but no precipitins to ovalbumin were detected. Lung function, X-ray and haematology provided no evidence that the inhalation of egg had lasting detrimental effects.

There was no correlation between clinical response, skin testing, IgE levels and precipitins, hence, for each individual none of these parameters is predictive. However, collectively the results show sensitization and this has been confirmed by lack of symptoms when a different method of coating the pastry was adopted.

Introduction

Hypersensitivity to egg materials is not uncommon, indeed, the egg component ovalbumin (OVA) is considered to be one of the most important food allergens (Gavani, Hyde & Moore, 1978; Beers, 1965). Apart from a few cases of dermatitis caused by handling eggs (Rudzki & Grzywa, 1977) nearly all other hypersensitivity reactions described have occurred when eggs or egg products are ingested by individuals intolerant to egg protein. Egg-specific IgE antibodies, usually determined against OVA, are found in the sera of these cases although their presence does not necessarily correlate with a state of intolerance (Gavani *et al.*, 1978; May *et al.*, 1977).

Eggs also contain proteins that have been associated with extrinsic allergic
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alveolitis (EAA) (Reed, Sosman & Barbee, 1965; Edwards, Barboriak & Fink, 1970) and inhalation challenge with these proteins (Moore *et al.*, 1974) has evoked the late influenza like symptoms that characterize EAA. Whereas most cases of EAA to avian protein are caused by inhaling pigeon or budgie protein (Hendrick, Faux & Marshall, 1978) some cases of EAA to chicken protein have been described in poultry workers (Warren & Tse, 1974).

Egg proteins, OVA (Gadaleanu, 1982) and egg albumen (Eastham & Muller, 1972) introduced into the lungs of experimental animals have induced pulmonary lesions consistent with mixed immunological responses. Immediate (type I) hypersensitivity; late, (Arthus, or type III) reactions (Eastham & Muller, 1972; Santives *et al.*, 1976) have been described and a chronic hypersensitivity pneumonitis state has been achieved by introducing a combination of OVA and muramyl dipeptide into the lungs of sensitized animals (Richerson *et al.*, 1982).

It was, therefore, of great interest when we were able to investigate the human response to inhaled egg material.

Materials and methods

Subjects and exposure pattern

Thirteen bakery workers (all female) were investigated at the MRC Pneumoconiosis Unit, Llandough Hospital.

They had been using chicken egg solution with or without the dye Egyelo (a mixture of tartrazine and sunset yellow) a permitted food additive, as a glaze for meat rolls. The egg solution, approximately 25% mixed egg white and yolk in water, was originally brushed onto the meat rolls but in order to speed up the process a commercial paint spray gun operating from a compressed air line was installed. Surplus egg spray easily found its way into the atmosphere and was inhaled by the operatives. Due to the shift system and other allocated tasks, over 2 working weeks, the workers were exposed to the egg spray on five occasions for periods of up to 75 min. The use of face masks was suggested but was not always implemented by the operatives.

Investigations

A clinical history was obtained from each operative using the standard MRC questionnaire of respiratory symptoms. Additional questions relating to symptoms experienced at work and to intolerance towards eggs or egg products were asked, as well as personal and family history of allergy and other avian contact.

Radiology. Standard chest X-rays were taken.

Lung function. The following parameters were determined: forced expiratory volume in 1 sec (FEV₁), forced vital capacity (FVC) before and after bronchodilator using a McDermott bellows spirometer, flow volume loops, lung volumes by helium dilution and single breath gas transfer factor (TL_{co}).

Haematology. Two millilitres were used for full blood count, differential and erythrocyte sedimentation rate.

Skin testing. Skin prick tests were performed using the common allergens, house dust, *Dermatophagoides pteronyssinus*, grass pollens, tree pollens, cat's fur and *Aspergillus fumigatus* (Bencard, U.K.). Subjects were also tested with specific antigens egg yolk, egg white and chicken serum each at 1/10 and 1/100 in saline with 33% glycerol. Chicken materials were heated at 56°C for 30 min prior to dilution. Egyelo

was also used for skin testing. Skin tests were read at 15 min when a weal 2 mm greater than control was taken as a positive result.

Serology. Serum was used for double-gel-diffusion testing (Working Party of the British Society for Mycopathology, 1976) against egg yolk, egg white and chicken serum each diluted 1/50 in saline. At the same time 200 random sera from the Blood Transfusion service were similarly tested. Total IgE was determined on each sample by paper radioimmunosorbant test (PRIST) and OVA-specific IgE by radioallergosorbant test (RAST) (Pharmacia). Sera from three other groups of individuals were also included in PRIST and RAST tests. These were a group of six non-atopics (skin test negative to the six common allergens); six atopics (skin test positive to two or more of the six common allergens); six individuals with a previously recorded skin test positivity to egg of greater than 4 mm above control.

Results

Clinical findings

Eight of the thirteen reported symptoms although there was no consistent definite pattern for all eight. Four experienced chest tightness, cough, wheeze and dyspnoea within $\frac{1}{2}$ to 1 hr of starting work with the egg spray. Two others had immediate symptoms of dry cough. One worker complained of dyspnoea, cough and nasal congestion that started about half an hour after work finished, i.e. about 2 hr after first exposure and for one worker the symptoms were vague and irregular, marked as $\pm$ on Table 1. No workers experienced late pyrexial episodes or other influenza-like symptoms. The symptoms resolved gradually, i.e. up to 5 hr, although a nocturnal cough persisted but by the next day all were symptom free.

There was little difference in mean age between symptomatic (39.5 ± 9.2 years) and

Table 1. Summary of responses and immunological findings in thirteen bakery workers exposed to egg aerosol

Subject	Response to inhaled egg	Skin test to one or more common antigens	Skin test to egg	Total IgE (iu/ml)	IgE to OVA (iu/ml)	Precipitins to egg yolk, white or chicken serum
J.A.	+	+	+	672	3	—
A.B.	—	+	—	54	0	—
B.C.	+	+	—	160	1	+
D.M.	+	—	—	26	0	—
E.F.	$\pm$	—	—	11	0	(+)
G.F.	—	—	—	<5	0	++
L.J.	—	—	—	9	0	+++
A.J.	—	+	+	84	3	(+)
F.J.	+	+	—	24	0	++
M.L.	+	—	—	6	0	—
S.M.	+	—	—	<5	0	+
E.S.	—	—	—	160	1	+
C.T.	+	+	—	19	0	++

Key (+), weak; +, positive; ++, moderate positive; +++, strong positive.

asymptomatic (44.4 ± 6.3 years) persons, although the symptomatic group had been at the factory for a shorter period than the asymptomatic group (23.5 ± 12.1 months *v.* 42.2 ± 8.1 months) and had less exposure to the egg spray (15.5 ± 10.6 months *v.* 29.4 ± 16.5 months).

Six of the eight symptomatic and two of the five asymptomatic persons gave a history of allergy to other substances. Two workers gave a history of intolerance to ingested cooked egg, one symptomatic, one asymptomatic.

Three of the eight symptomatic and four of the five asymptomatic persons smoked. Analysis of the MRC questionnaires showed that for the asymptomatic group all those with cough, wheeze and dyspnoea were smokers whereas for the symptomatics four non-smokers had such symptoms.

Chest X-ray. All chest X-rays were within normal limits.

Lung function. Lung function was abnormal in one case—a symptomatic smoker with a history of allergy and positive skin test reactions to several allergens. This subject had a pattern consistent with reversible obstructive airways disease.

Haematology. All haematological results were within normal limits.

Skin testing. Six of the thirteen were positive to one or more common allergens (Table 1) (four symptomatic and two asymptomatic persons) but only two of the thirteen responded to chicken proteins, one had symptoms, one was asymptomatic. All thirteen were negative to Egyelo.

Serology. Nine of the thirteen subjects (five symptomatic and four asymptomatic) reacted to one or more extract, egg yolk, white or chicken serum with varying degrees of positivity. Two were weakly positive to a single antigen in egg yolk, three were positive to one or more antigens and four were moderately to strongly positive to at least one antigen. Immunoelectrophoresis and specific gel diffusion testing with x5 crystalized OVA (Sigma) showed that the precipitin antibody response was not directed against this component of the protein mixture in the whole egg. None of the 200 sera from the Blood Transfusion Service, tested at the same time, were positive.

PRIST and RAST testing revealed four of the thirteen to have levels of IgE greater than 80 iu/ml serum and all four had specific IgE antibodies to OVA. However, two were symptomatic, two asymptomatic (Table 1).

In the additional groups, as might be expected, the atopic persons (five out of six) and those positive to egg by skin test (five out of six) had increased IgE levels, none of the non-atopic persons had increased amounts of IgE. None of the sera in these additional groups had specific IgE antibodies to OVA.

Discussion

Our present findings of an immediate type pulmonary response as opposed to a late EAA type response to inhaled egg materials were somewhat contrary to expectations since eggs contain proteins previously associated with EAA (Reed *et al.*, 1965; Edwards *et al.*, 1970) and particularly since the presence of precipitins usually a characteristic of EAA were found in most (nine out of thirteen) sera from exposed workers.

It is difficult to reconcile our findings with the concept of an immediate, type I, reaction being required to initiate a later Arthus, type III, reaction by allowing the influx of precipitins into the reacting area due to increased vascular permeability (Santives *et al.*, 1976). Four of the eight symptomatic patients had both immediate symptoms and precipitins but in none of these were the late type III reactions observed.

This concept had in some ways been suspect since we have observed in other studies (Cockcroft *et al.*, 1981) late skin test reactions consistent in time course and nature with previously described type III skin responses but in individuals without detectable precipitins (Edwards & Cockcroft, 1981).

As far as we are aware immune stimulation in man by eggs produces only immediate type allergy either by ingestion (Beers, 1965), contact (Rudzki & Grzywa, 1977), or inhalation. An analysis of skin test results on other groups (data kindly supplied by Dr B.H. Davies, Director, Asthma Research Unit, Sully Hospital, S. Glamorgan) shows that all individuals skin test positive to eggs also have a positive skin reaction to one or more common allergens suggesting that those ultimately developing skin test reactivity by ingestion are pre-disposed to sensitization by common allergens. In contrast, inhalation of egg material evokes immediate reactions in atopics and non-atopics equally, a finding also observed in our studies on animal handlers (Cockcroft *et al.*, 1981). The clinical significance of a positive skin test to eggs is dubious, none of the subjects in the serological control group that were skin test positive to eggs referred to intolerance to ingested egg, neither did the two skin test positives in the bakery workers. There is little from our work to link skin test reactivity and oral or inhalation sensitivity to eggs although this is not necessarily the case for all studies on egg sensitivity (Gavani *et al.*, 1978).

An important finding was that none of the exposed workers formed precipitin antibody against OVA and other workers have commented on the poor immunogenicity of this protein when used without adjuvant (Gadaleanu, 1982). This raises doubts as to the value of experimental pulmonary pathology induced by OVA as a model of EAA (Santives *et al.*, 1976). The lesions that have been induced experimentally are usually in animals previously immunized with OVA in adjuvant (Gadaleanu, 1982; Santives *et al.*, 1976; Richerson *et al.*, 1982). One study of pulmonary exposure to egg albumin alone showed animals to respond with features consistent with both immediate and Arthus-like reactions after multiple exposures (Eastham & Muller, 1972).

Our observations were that the precipitin antibody response was mainly to yolk components and all subjects with antibodies reacted with one yolk component, indeed, two reacted only to this component. It may be the case that this antigen represents a better immunological agent to be used than OVA when immune responses to egg are under investigation.

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