Evaluation of Occupational Asthma from Airborne Egg Protein Exposure in Multiple Settings*

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We previously reported IgE-mediated occupational asthma among workers exposed to airborne egg protein at a plant that produces liquid and dried powdered egg products. To demonstrate that our original observations are generalizable to other facilities that process eggs, and to estimate the prevalence of IgE-mediated occupational asthma among egg-exposed workers, we conducted surveys at two additional plants. We administered a questionnaire to 188 employees to identify workers with symptoms suggestive of occupational asthma. We further evaluated 88 workers with and without symptoms by a clinical examination by a physician blinded to results of other tests, serial peak expiratory flow rate (PEFR) determinations every three hours while awake for one week, and skin prick tests and serum specific IgE levels to extracts of factory egg products, commercial egg test reagents, and egg white protein fractions. Fourteen workers had work-related asthmalike symptoms by questionnaire, a physician diagnosis of occupational asthma, and evidence of IgE-mediated sensitization to one or more egg proteins. Workers exposed exclusively to liquid egg aerosol, as well as workers exposed primarily to dried airborne egg protein, developed occupational asthma. This study replicated our original observations and demonstrated that workers in all areas of liquid and powdered egg production are at risk of developing occupational asthma from exposure to airborne egg proteins.

(Chest 1990; 98:398-404)

ACGIH = American Conference of Governmental Industrial Hygienists; H_2SO_4 = sulfuric acid; $NaHCO_3$ = sodium bicarbonate; NIOSH = National Institute for Occupational Safety and Health; NOA = nonoccupational asthma; OA = occupational asthma; OSHA = Occupational Safety and Health Administration; PEFR = peak expiratory flow rate; PEL = permissible exposure limit; RAST = radioallergosorbent test; TLV = threshold limit value; TWA = time weighted average

More than 200 chemical and biologic agents have been demonstrated to cause occupational asthma,[1] and more inevitably will be identified.[2] In 1987 we reported IgE-mediated occupational asthma among workers at a factory, which we will refer to as "plant 1," where eggs were broken, the whites and yolks separated, and liquid and powdered dried egg products were produced.[3-5] Until this report, occupational asthma associated with immediate hypersensitivity to airborne egg proteins had not previously been demonstrated in this industry. However, bakery workers using an aqueous egg solution as a glaze for meat rolls had previously been reported to experience asthmalike symptoms.[6]

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To determine whether the original observations were generalizable to all plants that break, separate, and dry eggs, we conducted similar medical and industrial hygiene surveys at two additional facilities, which we will refer to as plants "2" and "3". Workers at plant 2 were exposed only to liquid raw egg products, while workers at plant 3 were potentially exposed to both liquid egg aerosols and dried egg products.

Methods

Plant Descriptions

The processes at plant 2 and plant 3 were similar to those previously described for plant 1,[4] and they are more fully described in technical reports available from the National Institute for Occupational Safety and Health (NIOSH).[7,8] Both plants 2 and 3 produced liquid egg products. In addition, plant 3 dried liquid whole eggs, yolks, and whites. In the "transfer" rooms of either plant, eggs were loaded onto continuous conveyers that traveled in sequence through washing machines, over inspection (or "candling") tables, and through windows into the adjacent breaking rooms, where the eggs were machine broken and separated. Sources of raw egg exposure included accidental breakage prior to and during washing. Visible egg-laden aerosol escaped from the washers and was also generated during breaking. At plant 3, sources of dried egg exposure included dust that had escaped from the drying ovens, separators, and sifters; blending operations; manual packaging operations; clean-up operations; and periodic manual cleaning of the ovens. Workers at plant 2 did not rotate between jobs during a

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Manuscript received September 22, 1989; revision accepted January 23, 1990.
No reprints available

work shift.[7] Once trained, workers at plant 3 tended not to rotate between liquid aerosol–exposed jobs (transfer and breaking rooms) and dried egg–exposed jobs (drying and packaging). Within the transfer room, workers rotated each hour during a work shift.[8]

Environmental Assessment

We conducted air sampling in the transfer and breaking rooms at plants 2 and 3 and in the drying and packaging areas of plant 3. Area samples collected using midget impingers containing 20 ml of $NaHCO_3$ were analyzed for chloride ions, released by a sanitizing agent sprayed on eggs exiting the washing machines. Area samples collected using silica gel solid sorbent tubes were analyzed for acid gases (HCl and H_2SO_4), constituents of cleaning products used in the plant. Both sets of analyses followed NIOSH method 7903, using an ion chromatograph (DIONEX 2010i).[9] We collected personal (breathing zone) air samples on 37-mm glass fiber filters and analyzed them for total protein by the Micro-Kjeldhal method.[10] Area air samples obtained near dried egg operations at plant 3 were analyzed for total and respirable protein. Separate bulk samples of clean and dirty wash water were obtained from the washing machines and were analyzed for total protein.

Medical Survey

Survey procedures were approved by the NIOSH Human Subjects Review Board and were similar to those previously described.[4,5] We administered a questionnaire (reproduced in its entirety in a report[11] available from the National Technical Information Service) to every available employee, to identify workers with work-related wheezing, shortness of breath, or chest tightness suggestive of occupational asthma. As previously described,[4] we suspected a respondent might have occupational asthma if he or she reported having experienced within the preceding month wheezy or whistling respiration or episodes of shortness of breath or chest tightness, and the symptom(s) occurred following specific activities or exposures at work, and on days away from work the symptom(s) occurred less frequently or not at all. We invited all respondents with work-related respiratory symptoms, and an approximately equal number of asymptomatic respondents, to participate in follow-up examinations.

A physician, blinded to results of all other procedures, examined each follow-up participant and rendered an opinion whether the participant had occupational asthma, nonoccupational asthma, or work-related irritant respiratory symptoms. Peak expiratory flow rates (PEFR) were measured every three hours while awake over a full week using Wright's portable mini-peak flow meters. Concomitant symptoms of wheezing, shortness of breath, chest tightness, and cough were recorded with each determination.[4] A difference between the daily maximum and minimum PEFR of 20 percent or greater of the daily maximum was taken as indirect evidence of reversible airways obstruction.[12] Symptomatic airways obstruction was diagnosed if wheezing, shortness of breath, or chest tightness were reported at the time the PEFR reached its daily minimum. Since the PEFR data were considered informative only if positive, inadequate data (*ie*, on three or fewer days) were equated with negative determinations.

We developed an egg allergen skin test panel that consisted of ten reagents from several sources, including commercial food allergens, purified egg white fractions, and extracts of powdered factory egg products.[5] Commercial food testing reagents (1:10 W/V) included solutions of egg white, egg yolk, and whole egg (Hollister-Stier, Spokane, Wash). Purified lyophylized egg white fractions, which included ovalbumin, conalbumin, lysozyme, and ovomucoid (Sigma Chemical Company, St. Louis, Mo), were diluted in phosphate-buffered saline solution (PBS) to a final concentration of 10 mg/ml. All fractions were sterilized through a polymer (Millipore) filter (Millipore Corporation, Bedford, Mass). Whole egg, egg whites, and egg yolk products obtained from each respective egg factory were dissolved in PBS at a concentration of 10 mg/ml (wt/vol). Undissolved material was removed by centrifugation. The supernatants were then filtered through a 0.45-μm polymer filter followed by filtration through a 0.22-μm polymer filter into sterile vials. Skin prick testing was also performed with a panel of commercial aeroallergens consisting of short ragweed, Kentucky bluegrass, timothy grass, cat, house dust mites, *Alternaria tenuis*, and hormodendrum (Hollister-Stier, Spokane, Wash). Control skin tests included PBS and histamine (1 mg/ml). A positive skin test was defined as a wheal and flare response with a wheal measuring 3 mm greater than the saline control. Atopic status was predefined by the presence of positive skin tests to two or more of the panel of common inhalant aeroallergens.

Specific IgE antibody to the various egg allergens was determined using a modification of the radioallergosorbent test (RAST). As described in the previous study, the solid phase RAST disks were prepared with factory-powdered whole eggs, egg whites and egg yolks, as well as with purified egg white fractions of ovalbumin, lysozyme, conalbumin, and ovomucoid at 10 mg/ml (Sigma Chemical Company, St. Louis, Mo). A commercial food egg white allergen disk (Pharmacia, Piscataway, NJ) was also included in the RAST panel. Approximately 10 mg/ml of protein antigen was coupled to methylcellulose disks activated with cyanogen bromide. The allergen disks were incubated with workers' serum samples for three hours at room temperature. After washing three times with PBS-Tween (polysorbate), the disks were reacted with 50,000 cpm of ^{125}I-labeled goat anti-human IgE antibody (Kirkegard-Perry Laboratories, Gaithersberg, Md) for 18 hours. After a final wash with PBS-Tween, the counts per minute of ^{125}I-anti-IgE bound were measured. A positive test was arbitrarily defined as counts per minute bound that were greater than 3 SDs above the mean binding of ten laboratory control subjects who were never exposed to egg antigens by inhalation.

Results

Environmental Survey

At both plants 2 and 3, air levels of chloride ions, for which there are no air exposure standards, were less than 0.065 mg/cu m. Acid gases were nondetectable, except for one sample each of hydrogen chloride (0.06 mg/cu m) and sulfuric acid (0.48 mg/cu m). The Occupational Safety and Health Administration's (OSHA) permissible exposure limit (PEL) and the American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit value (TLV) for hydrogen chloride are both 7 mg/cu m as a ceiling level, not to be exceeded at any time. The OSHA PEL and ACGIH TLV for sulfuric acid are both 1 mg/cu m as time-weighted averages (TWA) over eight hours.[13,14]

Personal and area air sample results for protein are summarized in Tables 1 and 2. In the transfer and

Table 1—*Personal Air Samples for Total Protein Level*

	Plant 2, mg/cu m	Plant 3, mg/cu m
Transfer room	0.39, 0.44, 0.60, 0.63, 0.73, 1.2	0.31, 0.37, 0.37, 0.40, 0.42, 0.48, 0.48
Breaking room	0.52, 0.69, 0.70, 0.93	0.17, 0.25, 0.38
Egg yellow dryer		0.37, 0.72
Egg white dryer		10.0
Packaging (dried products)		11.0, 31.0, 132.0

Table 2—*Area Air Samples for Total and Respirable Protein Level (Plant 3 only)*

	Total, mg/cu m	Respirable, mg/cu m
Yellow dryer area	0.23, 0.30	0.22, 0.40
White dryer area	8.0, 25.0	0.72, 0.77
Packaging area	32.0	0.35, 0.41

breaking rooms of both plants, all air levels were less than 1.2 mg/cu m. At plant 3, all five air samples for protein in the dried egg "yellow" (whole egg or egg yolk) exposed areas were less than 0.72 mg/cu m. In contrast, only one of eight air samples for total protein in the dried egg white exposed areas and the packaging areas was less than 8 mg/cu m, while respirable protein levels in these areas were all less than 0.77 mg/cu m. The only applicable exposure standards are the OSHA PELs and the ACGIH TLVs for total and respirable dust. The OSHA PELs are 15 mg/cu m for total and 5 mg/cu m for respirable dust. The respective ACGIH TLVs are 10 mg/cu m and 5 mg/cu m.[12,13]

At plant 2, over the course of a work shift, protein concentration in recirculated water from the egg washers increased from 0.27 to 5.6 mg/ml. At plant 3, protein in wash water increased from 0.1 to 1.0 mg/ml.

Medical Survey

Ninety-two (86 percent) of 107 employees at plant 2, and 96 (97 percent) of 99 employees at plant 3 responded to the questionnaire. Subsequent inquiries revealed that none of the nonresponders was absent due to work-related respiratory disease. Fifty-eight respondents reported by questionnaire work-related wheezing, shortness of breath, or chest tightness. Twenty-five reported episodic symptoms, not work related. One hundred and five workers reported no such symptoms. Forty-four (83 percent) of 58 respondents who reported work-related symptoms, and 44 (78 percent) of 51 invitees without such symptoms, participated in the medical follow-up. Table 3 lists participants cross classified by work-related symptoms elicited on questionnaire, physician's evaluation, symptomatic variability in PEFR, and skin test reactivity to egg proteins. Table 4 lists pertinent survey data for each participant.

The questionnaire identified work-related respiratory symptoms in 35 of 37 participants diagnosed by the physician to have occupational asthma or work-related irritant symptoms, compared with nine of 51 diagnosed by the physician to have nonoccupational asthma or other (including no) respiratory symptoms (Fisher's exact test, $p<0.0001$). The sensitivity and specificity of the questionnaire for the physician's diagnosis of work-related respiratory symptoms (occupational asthma or irritant symptoms) were 95 percent (35/37) and 82 percent (42/51), respectively.

Peak flow rate determinations revealed symptomatic PEFR variability in 18 of 37 participants diagnosed by the physician to have asthma, either occupational

Table 3—*Follow-up Examination Participants Cross-Classified by Questionnaire Response, Physician's Diagnosis, Peak Expiratory Flow Data, and Skin Tests to Egg Proteins**

Questionnaire: Work-related Symptoms	Physician Diagnosis	PEFR: Airways Hyperreactivity	At Least Two Positive Skin Tests	One Positive Skin Test	No Positive Skin Tests	Total
	OA	Yes	5	2	5	12
		No	9	0	6	15
	NOA	Yes	1	0	3	4
		No	0	0	1	1
Yes	IRR	Yes	0	0	0	0
		No	0	0	8	8
	Other	Yes	0	0	0	0
		No	0	0	4	4
	OA	Yes	0	0	1	1
		No	0	0	0	0
	NOA	Yes	0	0	1	1
		No	0	0	3	3
No	IRR	Yes	0	0	0	0
		No	0	0	1	1
	Other	Yes	0	0	1	1
		No	8	4	23	35†
Total			23	6	57	86

*OA = occupational asthma; NOA = nonoccupational asthma; IRR = irritant respiratory symptoms; Other = other symptoms, including no symptoms.

†Skin tests were not performed on two individuals who denied work-related respiratory symptoms, were not considered by the physician to have OA, NOA, or irritant symptoms, and whose peak flow data were negative for PEFR variability.

Table 4—*Skin Test Antigens or RASTs that Resulted in Positive Test Results**

ID	Work-Related Symptoms	MD Dx	PEFR Percent Daily Variation, Range	Symptomatic Bronchial Hyperreactivity	Skin Tests	RASTs
1	Yes	OA/IRR	9-38	Yes	WE,EW,EY,OVA,CON,LYS,FWE,FEW,FEY	
2	Yes	OA	12-36	Yes	WE,EW,EY,OVA,CON,LYS,OVM,FWE,FEW	CON,LYS,OVM,FWE
3	Yes	OA	3-28	Yes	EW,EY,OVA,CON,OVM,FWE,FEW,FEY	
4	Yes	OA	20-31	Yes	WE,CON,LYS,OVM,FEY,FEW	
5	Yes	OA/IRR	6-30	Yes	EW,OVA,FWE,FEW	
6	Yes	OA/IRR	5-41	Yes	EY	LYS
7	Yes	OA	4-27	Yes	OVM	
8	Yes	OA/IRR	5-33	Yes		
9	Yes	OA	15-20	Yes		
10	Yes	OA	10-26	Yes		
11	Yes	OA	39-48	Yes		
12	Yes	OA	2-22	Yes		OVM
13	Yes	OA	15-21	No	WE,EW,EY,OVA,CON,LYS,OVM,FWE	
14	Yes	OA	2-12	No	EW,OVA,CON,LYS,OVM,FWE	CON,LYS,OVM,FEW
15	Yes	OA	2-9	No	WE,EW,OVA,CON	CON,LYS
16	Yes	OA	2-11	No	WE,EW,EY,LYS	
17	Yes	OA	Missing		WE,EY,OVA	CON
18	Yes	OA	7-16	No	CON,LYS,OVM	OVM
19	Yes	OA	3-14	No	WE,EW,OVA	
20	Yes	OA	8-16	No	EW,OVA	CON,LYS,OVM,FWE,FEW
21	Yes	OA	4-18	No	OVA,LYS	LYS,OVM,FWE
22	Yes	OA/IRR	3-14	No		Missing
23	Yes	OA/IRR	3-9	No		
24	Yes	OA/IRR	2-5	No		FWE
25	Yes	OA/NOA	1-5	No		
26	Yes	OA/IRR	5-18	No		
27	Yes	OA	5-13	No		
28	Yes	NOA	9-44	Yes	EW,EY,OVA,CON,LYS,OVM	CON,LYS,OVM,FWE
29	Yes	NOA	14-26	Yes		LYS
30	Yes	NOA	6-25	Yes		
31	Yes	NOA	3-29	Yes		
32	Yes	NOA	Missing			
33	Yes	IRR	Missing	Yes		FWE
34	Yes	IRR	4-10	No		
35	Yes	IRR	4-11	No		
36	Yes	IRR	Missing			
37	Yes	IRR	1-5	No		
38	Yes	IRR	2-12	No		
39	Yes	IRR	3-12	No		FEW
40	Yes	IRR	7-11	No		
41	Yes	Other	4-12	No		
42	Yes	Other	Missing			
43	Yes	Other	2-7	No		OVM
44	Yes	Other	3-16	No		
49	No	OA	4-21	Yes		
45	No	NOA	3-33	Yes		
46	No	NOA	2-19	No		
47	No	NOA	7-18	No		
48	No	NOA	3-8	No		
70	No	IRR	3-11	No		
50	No	Other	2-20	Yes		
51	No	Other	Missing		WE,EW,EY,CON,LYS,OVM,FWE,FEW	CON,LYS,FEW
52	No	Other	4-15	No	WE,EW,EY,CON,LYS,FWE,FEW	CON,LYS,OVM,FWE,FEW
53	No	Other	3-11	No	WE,EW,EY,CON,FWE	
54	No	Other	Missing		EW,EY,CON,LYS,FWE	FEW
55	No	Other	3-10	No	EW,CON,FWE	FWE,FEW
56	No	Other	8-14	No	WE,EW,CON	CON
57	No	Other	1-7	No	EW,LYS,FEW	

(Continued on next page)

Table 4, *Continued*

58	No	Other	2-17	No	WE,EW	
59	No	Other	4-26	No	EY	
60	No	Other	Missing		CON	
61	No	Other	3-9	No	LYS	
62	No	Other	Missing		WE	
63	No	Other	6-10	No		FWE
76	No	Other	Missing			LYS
86	No	Other	Missing			CON

*RAST = radioallergosorbent test; FWE = factory whole egg; FEW = factory egg white; FEY = factory egg yolk; WE = whole egg (Hollister-Stier); EW = egg white (Hollister-Stier); EY = egg yolk (Hollister-Stier); CON = conalbumin; OVA = ovalbumin; OVM = ovomucoid; LYZ = lysozyme; PEFR = peak expiratory flow rate; MD Dx = physician diagnosis; OA = occupational asthma; NOA = nonoccupational asthma; IRR = irritant respiratory symptoms; Other = other symptoms, including no symptoms.

Twenty-two observations were deleted. None of the 22 had work-related symptoms by questionnaire or physician diagnoses of asthma or irritant symptoms. Thirteen of 22 had no evidence of airways hyperreactivity by PEFR. Nine had missing or inadequate PEFR data.

or nonoccupational, compared with one of 51 diagnosed to have either irritant symptoms or other (including no) symptoms (Fisher's exact test $p<0.0001$). The sensitivity and specificity of the peak flow data for the physician's diagnosis of asthma (occupational or nonoccupational) were 49 percent (18/37) and 98 percent (51/52), respectively.

Among 86 workers in whom skin tests were performed, there were 29 (34 percent) with cutaneous sensitization to one or more egg protein allergens. Evidence for allergy to egg proteins was compared for participants dually concordant for work-related symptoms by questionnaire and the physician's diagnosis of occupational asthma, and for participants not so concordant. Table 5 summarizes allergy to egg proteins for both groups by increasingly restrictive criteria, namely, at least one or two positive skin tests or RASTs. Skin test positivity to egg proteins was significantly associated with dual concordance for work-related respiratory symptoms and a diagnosis of occupational asthma, while RAST positivity was not. Sixteen (59 percent) of 27 participants for whom there was dual concordance between questionnaire responses for work-related symptoms, and the physician's diagnosis of occupational asthma, had at least one positive skin test to egg proteins, compared with 13 (22 percent) of 59 who were not dually concordant ($\chi^2=9.88$, $p=0.0016$). Fourteen of 27 dually concordant participants had at least two positive skin tests, compared with eight of 59 not concordant ($\chi^2=10.9$, $p=0.0010$). While RAST positivity was not significantly associated with dual concordance for work-related symptoms and a diagnosis of occupational asthma, nevertheless, all participants with two or more positive RASTs also had two or more positive skin tests. Of 29 workers with cutaneous reactivity to at least one egg allergen, 16 (55 percent) exhibited a positive RAST.

Based on the foregoing, we concluded that the 14 participants who had work-related symptoms on questionnaire, who were diagnosed by the physician to have occupational asthma, and who had two or more positive skin tests to egg proteins, indeed had "egg" asthma. The peak flow data were deemed informative only if symptomatic variability in lung function was demonstrated. Because it could not be ascertained that negative peak flow determinations excluded the possibility of asthma, we did not incorporate this parameter into the overall diagnosis of egg asthma. By this criterion, 10 percent (9/92) of workers at plant 2 and 5 percent (5/96) of workers at plant 3 had "egg asthma."

Table 6 summarizes, by work areas at both plants combined, the numbers of questionnaire respondents, numbers of "egg asthmatics," and estimated minimum prevalences of egg asthma. The prevalences among raw egg-exposed workers (transfer room and breaking room employees) were 12 percent and 10 percent, respectively. The prevalence among dried egg-exposed workers (plant 3 only) was 5 percent. There was one

Table 5—*Summary of Allergy to Egg Proteins for Both Groups by Increasingly Restrictive Criteria*

Criteria for Allergy to Egg Protein	Proportion (percent) Positive among Dually Concordant* Participants	Proportion (percent) Positive among Participants Not Dually Concordant	Test Statistic
≥1 Positive skin test	16/27 (59%)	13/59 (22%)	$\chi^2=9.88$, $p=0.0016$
≥2 Positive skin tests	14/27 (52%)	9/59 (15%)	$\chi^2=10.9$, $p=0.0010$
≥1 Positive RAST†	11/27 (41%)	14/59 (24%)	$\chi^2=1.84$, $p=0.17$
≥2 Positive RASTs	5/27 (18%)	4/59 (7%)	Fisher's exact $p=0.10$

*Work-related respiratory symptoms by questionnaire and the physician's diagnosis of occupational asthma.

†RAST = radioallergosorbent test.

Table 6—*Estimated Prevalence of Egg-Asthma by Work Area*

Work Area	Total No. of Workers	No. of Egg Asthma	Estimated Prevalence of Egg Asthma
Administrative	11	1	9%
Warehouse	7	0	0%
Transfer room	69	8	12%
Breaking room	44	4	10%
Dried egg products (plant 3 only)	20	1	5%
Maintenance and clean-up	28	0	0%
Other	9	0	0%
Total	188	14	7%

egg asthmatic among administrative personnel who attributed his symptoms to egg white dust from the dryer at plant 3, which he consequently avoided.

Among follow-up participants at plants 2 and 3, there was no association between atopy and prevalence of egg asthma. Four (29 percent) of 14 egg asthmatics were atopic compared with 17 (19 percent) of 72 workers not so classified (Fisher's exact test, $p = 0.46$).

Discussion

These studies documented that IgE-mediated sensitization to egg protein occurs among workers exposed both to raw egg aerosols and to dried egg products in the egg processing industry. Mindful that the occurrence of occupational asthma may be a sentinel event that reveals the need to search for additional cases within the industry and for remediable underlying causes of disease,[15,16] our original epidemiologic study was replicated, and IgE-mediated egg asthma was found in both facilities studied. Combined data presented in this report from two egg processing facilities confirm earlier observations.[5] In the present investigation, IgE-mediated cutaneous sensitization to egg protein allergens was demonstrated among 34 percent of egg-exposed workers and is in agreement with a 32 percent prevalence of cutaneous sensitization detected in the original study. It is noteworthy that 13 (45 percent) of 29 skin test–positive workers did not satisfy criteria for diagnosis of occupational asthma as defined by dual concordance between the physician diagnosis of occupational asthma and work-related respiratory symptoms elicited by questionnaire. This suggests that cutaneous sensitization to egg proteins can occur commonly among asymptomatic workers in this setting. However, based on the higher prevalence of cutaneous reactivity among workers that satisfied dual concordance criteria vs those who did not, it can be concluded that cutaneous reactivity to egg proteins is associated with occupational asthma. A positive skin test to egg protein allergens in itself does not establish a diagnosis of occupational asthma but it is a useful screening method for surveillance of workers and may aid in identification of individuals at risk for development of IgE-mediated occupational asthma. To determine the predictive value of the skin test, longitudinal studies of egg processing workers would be required.

Only 55 percent of workers with cutaneous reactivity to at least one egg allergen had at least one positive RAST compared with 50 percent previously. Further, there was no significant association between RAST positivity to egg allergens and dual concordance between the questionnaire and physician diagnosis. This could be a result of lesser sensitivity of the RAST assay in comparison to epicutaneous testing for detection of specific IgE responses.[17]

Although we replicated our previous study, we eliminated from our protocol previously used methods we had found to be uninformative. We did attempt to identify airways obstruction using forced spirometry, since in our previous study this was both time consuming and had a low sensitivity (40 percent) for egg asthma.[4] As well, we did not measure specific IgG antibody to egg proteins. We previously determined that mean levels of IgG antibodies of egg-exposed workers were two to three times greater than those of non-egg-exposed controls. Yet virtually all egg-exposed workers were IgG positive to at least one egg protein, and IgG levels did not differentiate symptomatic from asymptomatic workers. IgG antibodies to egg proteins appeared to be an index of exposure rather than effect.[5]

Various methods in this study were cross-validated with respect to sensitivity and specificity. Serial PEFR studies proved to be highly specific but lacked sensitivity for identification of workers with occupational asthma based on the physician's diagnosis. On the other hand, the questionnaire exhibited excellent sensitivity and good specificity for the physician's assessment of work-related respiratory symptoms. Depending on the choice of criteria, up to 10 percent of workers at each of three egg-processing plants have been determined to have egg asthma. To the extent that the criteria increase specificity but decrease sensitivity to identify egg asthma, the derived prevalence of occupational asthma among egg-exposed workers will be an underestimate. Since these investigations have used cross-sectional designs to determine the prevalence of egg asthma among currently exposed workers, biases due to self-selection and survivorship[18] may also contribute to an underestimation of the true prevalence of occupational asthma, both by plant and by job assignment within plant. Yet not every case of a disease must be identified to demonstrate that a problem exists that requires remediation.

When we initiated our original studies, there were 101 plants in the United States that processed raw

eggs or egg products and were under inspection by the US Department of Agriculture. There are now 85 such plants, and the three surveyed were among the ten largest in the country. If it is assumed that the typical workforce at these plants averages 50 workers, and that approximately 10 percent of workers at each plant may have occupational asthma from airborne egg protein exposure, then at any one time there could be as many as 425 prevalent cases of egg asthma among currently employed egg processing workers in the United States.

Air monitoring demonstrated that egg protein levels in liquid egg aerosol-exposed areas were within applicable standards and recommendations. Workers in egg-drying operations at plant 3 were exposed to total dust levels exceeding applicable standards, but the respirable fractions were all less than 1 mg/cu m, and below applicable standards and recommendations. However, as noted by the American Conference of Governmental Industrial Hygienists, these standards were not meant to "apply to those substances which may cause physiologic impairment at lower concentrations, and for which threshold limits have not yet been recommended."[19] This may be applicable to egg proteins that may result in allergic respiratory sensitization at relatively low airborne concentrations. Past experience among workers exposed to airborne proteolytic enzymes of *Bacillus subtilis* may offer some guidance in regard to a recommended exposure limit for airborne egg protein dust. Early studies of enzyme-exposed workers demonstrated the prevalence of occupational asthma to be comparable to that which we have observed among egg-exposed workers.[20] The ACGIH recommends that occupational exposure to proteolytic enzymes not exceed 0.06 μg/cu m at any time (*ie*, this is a "ceiling" limit).[14] It is likely that significant engineering controls will necessarily be exerted to reduce aerosol and dust exposures in egg-processing plants to levels at which allergic sensitization of unprotected workers will not be a problem.

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