

Farm animal feeders: another group affected by cereal flour asthma

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Asthma induced by cereal flour is a long recognized entity. We present studies of three patients affected by asthma related to exposure to cereal flour contained in animal formula feeds. Skin prick test performed with the formula feed components showed positive reactions to cereal flours (wheat, rye and barley) and negative to the other substances in these formulas. Specific anti-wheat, rye and barley flour IgE antibodies were found by RAST. Bronchial provocation tests (BPT) with wheat flour (patients 1 and 2) and barley flour (patient 3) all showed immediate responses. These findings suggest that our patients' symptoms were caused by an IgE-mediated hypersensitivity to cereal flours from animal formula feeds. We call attention to the importance of cereal flours in animal formula feeds as a cause of occupational asthma in farm animal feeders.

Key words: animal formula feeds; baker's asthma; bronchial provocation test (BPT); cereal flours; occupational asthma.

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Cereal flour asthma is an entity that has long been recognized. In 1713 Ramazzini gave the first scientific description of baker's asthma (11). Later, Schloss in 1916 and Walter & Cooke (6) obtained positive skin reactions to wheat extracts in patients with flour allergy, and de Besche in 1929 (2) reported on the successful Prausnitz-Kustner (P-K) test with the sera of workers allergic to wheat flour. In the following years numerous authors have been interested in the study of this type of occupational asthma, and specific IgE antibodies to cereal flour have been demonstrated in affected workers by *in vivo* and *in vitro* techniques (1, 4). However, asthma caused by cereals is not exclusive to bakers. Duke in 1935 (8) described sensitization to wheat hairs or surface scales as causing asthma in wheat flour mill workers, and de Besche (2) referred to P-K tests carried out in grain handlers hypersensitive to cereals.

Recently, we have studied three patients affected by respiratory symptoms related to farm animal feeding. Our investigations sug-

gested that cereal flour contained in these formula feeds was responsible for the referred symptoms.

Case 1

A 16-year-old boy student, without atopic family history was studied at our clinic. Since childhood he has had rhinitis and bronchial asthma during springtime. In the past 2 years his hobby has been horse riding and in the second year he noticed itching, rhinorrhea, dyspnea and wheezing on exposure to the formula horse feed. The symptoms persisted at night. When he avoided feeding his horse he was asymptomatic.

Clinical examination revealed expiratory wheezing over both pulmonary fields. Biochemical profile was normal. White blood cell count was 6450 with 420 eosinophils. Total IgE was 1000 IU/ml. Sinus X-ray revealed opacity of both maxilar antra. Chest X-ray was normal. Spirometric values were 86% for FEV₁ and 100% for FVC.

Case 2

A 54-year-old farm-worker (ex-smoker) had a 10-year history of nasal congestion, nasal itching, rhinorrhea and sneezing. During the last 8 years of this period he noticed also wheezing and dyspnea. In the last year his asthma symptoms became worse, sometimes requiring emergency hospital treatment. For many years he has been feeding cows with a commercial formula feed and he noticed that this activity impaired his respiratory symptoms.

Clinical examination and biochemical profile were normal. White blood cell count was 8740 with 520 eosinophils. Total IgE was 640 IU/ml. A cytologic examination of sputum revealed 70% eosinophils. Sinus X-ray showed mucosal thickening of right maxilar antra. Chest X-ray was normal. Spirometry revealed a FEV₁ of 81% and FVC of 86% predicted.

Case 3

A 19-year-old farm-worker (ex-smoker) with a family history of atopy was studied at our clinic. In the last 4 years he presented perennial nasal congestion, rhinorrhea and exercise dyspnea. A few minutes after exposure to home-made formula feed compounds used for cow fodder during the summer months, he experienced chest tightness, wheezing and dyspnea. Symptoms continued at night and he sometimes required emergency hospital treatment. In the last 2 years he has remained asymptomatic except when exposed to these compounds.

Clinical examination was normal. Total blood cell count and biochemistry were also normal. A cytologic examination of nasal smear showed 30% eosinophils. Total IgE was 320 IU/ml. Thorax and sinus X-ray were normal. Spirometry values were normal.

MATERIAL AND METHODS

For *in vivo* tests 2 grams of cereal flours (wheat, rye, barley and oat) were dissolved in 10 ml PBS (phosphate buffered saline), pH 7.3, at laboratory temperature. After stirring for 60 min and passing through filter paper, the solu-

tions were dialysed in PBS for 24 h and afterwards passed through a Millipore filter (Millipore Corp., Bedford, Mass.) for sterilization. These extracts were considered as a final concentration of 1:5 w/v. Several dilutions were made for skin and inhalation tests. Other animal formula feed components obtained from an animal feed company (Visan. Madrid. Spain), were prepared as described.

Skin prick tests were done with our own wheat, barley, rye and oat flour extracts (1:10 w/v). We also performed prick tests with the other components of commercial animal feeds (bone flour, animal fat, beet, alfalfa flour, soy bean and cotton) and 1:10 w/v. A battery of commercially available allergens including pollen, dust mites, storage mites, *Sitophilus granarius*, molds and horse and cow dander (Bencard, Betchworth, Surrey, U.K.) was tested. Ten normal subjects served as controls. We considered a reaction positive if the wheal size induced by the allergen was equal or larger than that produced by histamine phosphate 1 mg/ml. All skin tests were examined after 15 min and 4 to 8 h later.

The patients' sera were tested for precipitating antibodies to cereal flour extract dilutions by an agar gel diffusion method (10).

Specific IgE antibodies against wheat, rye and barley flour were measured by RAST technique according to the manufacturer's instructions (Pharmacia, Uppsala, Sweden).

Non-specific BPT with methacholine was performed following the method described by Cockcroft (7). The aerosolized particles were

Table 1
Skin prick test and RAST (PRU/ml) values in cereal flour extracts

Patient		Wheat flour	Rye flour	Barley flour
1	Prick	7 mm	6 mm	6 mm
	RAST	12	6	2
2	Prick	9 mm	9 mm	5 mm
	RAST	2.6	0.48	0.37
3	Prick	6 mm	12 mm	17 mm
	RAST	4.5	14	16.5

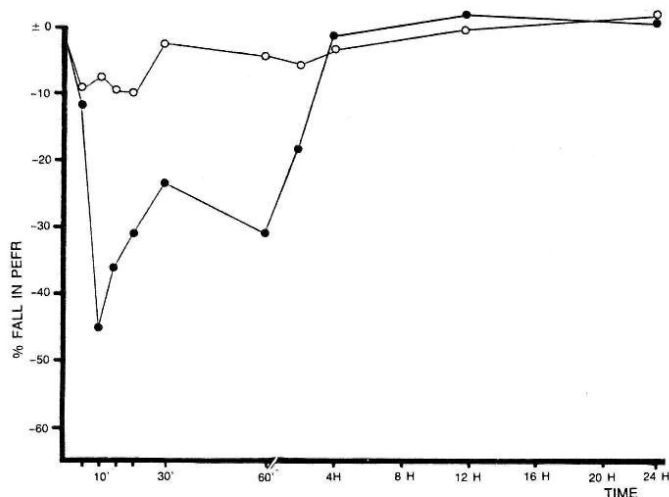


Fig. 1. ●—● Bronchial provocation test with wheat flour extract (1:5 w/v) in patient 1. ○—○ the same test after pretreatment with DSCG 40 mg.

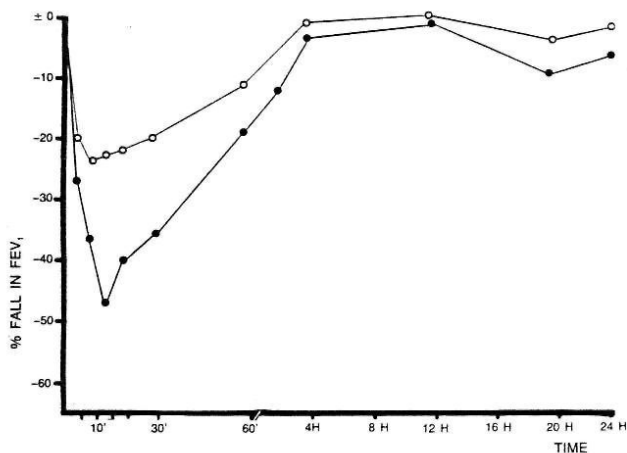


Fig. 2. ●—● Bronchial provocation test with wheat flour extract (1:10 w/v) in patient 2. ○—○ the same test after pretreatment with DSCG 40 mg.

generated by a continuous pressurized nebulizer model De Villbis 646, with a fitted output of 0.28 ml/min.

Specific BPT were done with wheat flour extract in patients 1 and 2 and with barley flour extract in patient 3.

The patients inhaled the aerosolized allergen in progressive concentrations for 2 min at normal breathing volume. A control challenge with

PBS was carried out before antigen challenge. Baseline pulmonary function measures of FEV_1 , FVC, and PEF were performed and repeated at 5, 10, 15, 30, and 60 min after each challenge. A positive immediate response was defined as a 20% or more fall in FEV_1 or 40% or more fall in PEF.

Hourly peak flow measurements were performed for 24 h following each challenge in

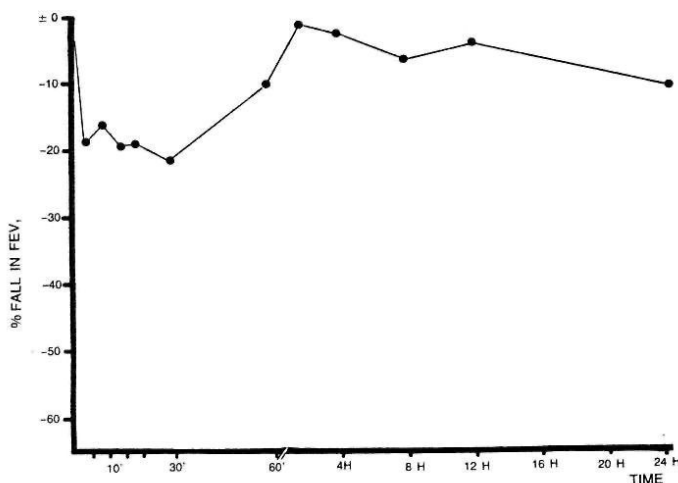


Fig. 3. ●—● Bronchial provocation test with barley flour extract (1:1000 w/v) in patient 3.

order to evaluate the late response. This was considered as a 40% or more fall in PEF from the baseline. The inhibitory effect of disodium cromoglycate (DSCG) on the inhalation reaction was also studied. DSCG (40 mg) was given by inhalation using a spinhaler 30 min before the provocation test.

Four non-exposed asthmatic patients were also challenged with 1:5 w/v cereal flour extract after obtaining informed consent.

RESULTS

After skin testing with cereal flour extracts patients exhibited positive responses with wheal and erythema after 15 min (Table 1). In contrast, control subjects showed no reaction tested gave negative responses in our patients. Neither the patients or control subjects had positive reactions to the commercially available allergens except patient 1 who had a positive response to pollen. Precipitins to cereal flour extracts were not found in patients' sera. Specific anti-cereal flour-IgE antibodies were found by RAST in all patients (Table 1).

Bronchial challenge with methacholine revealed severe bronchial hyperreactivity in the patients with PC_{20} of 0.35, 0.49 and 0.92 mg/ml respectively.

After challenge with wheat flour extract

patients 1 and 2 had an immediate and no late response (Figs. 1 and 2). After barley flour inhalation patient 3 showed also only an immediate response. (Fig. 3). Pretreatment with DSCG inhibited immediate asthmatic responses. Control subjects showed no reaction to bronchial challenge with cereal flour extracts.

DISCUSSION

The formula feeds used for animal fodder are composed of several nutrients, principally cereals. These feeds constitute the main current form of farm animal feeding.

Animal feeders are exposed to dust when handling these compounds. Daily exposure to cereal flours from formula feeds seemed to be the cause of hypersensitivity in our patients. Other sources of exposure to cereal flours were discarded. We showed by *in vivo* and *in vitro* tests that patients were only sensitized to cereal flours and not to the other formula feed components.

Sensitization to cereal flours in our patients can be due either to simultaneous environmental exposure or to cross-reactivity between cereals (3, 5).

In patient 1 we had observed cutaneous sensitivity to pollen with seasonal symptomatology several years before he began handling formula

feeds. Blands in 1976 (3), demonstrated that cereals and pollen share seven antigenic groups. Other authors suggest that pollinic subjects develop hypersensitivity to cereal flours with more frequency (9).

Our findings, together with the improvement of symptoms after the avoided animal feeding, suggest that the above described symptoms were caused by Type 1 IgE-mediated hypersensitivity to cereal flours from animal formula feeds.

We would like to draw attention to the potential importance of cereal flours in animal fodder as a cause of occupational asthma in animal feeders.

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