

Cheese workers' lung

SEVERAL cases of hypersensitivity pneumonitis (HP) have been described among cheese workers (1, 2). Systemic and respiratory symptoms occur several hours after exposure to moldy cheese, serum precipitins against *Penicillium* species are present, and bronchoalveolar lavage (BAL) analysis shows high-intensity lymphocytic alveolitis (3). In our study, BAL analysis was used in the follow-up of two patients with clinical evidence of cheese workers' HP.

■ *Case 1* was that of a 31-year-old man, never a smoker, who had worked for 16 years in the production and cleaning of cheese, and who had been seen for complaints of nocturnal fever, dyspnea,

Two cases of hypersensitivity pneumonitis to Penicillium analyzed by BAL.

and dry cough during the previous 3 years, related to exposure to moldy cheese. His chest radiograph and pulmonary function were normal. Skin prick tests with common inhalants were negative. Serum precipitins were evaluated by double immunodiffusion with a panel including the main HP antigens. Precipitins against *Penicillium notatum*, *P. viridicatum*, *Aspergillus fumigatus*, *A. niger*, and *Aureobasidium pullulans* were found. BAL and cyto-spin preparation were carried out as previously reported, and lymphocyte subsets were determined by flow cytometry (3). As shown in Table 1, BAL study demonstrated lymphocytic alveolitis, with reversed CD4/CD8 ratio and increased NK cells as defined by CD57⁺ cells. Transbronchial biopsy did not show any particular impairment. On the basis of exposure, clinical history, and serum precipitins, we diagnosed HP. The patient was still exposed and reported an acute episode of HP. Two years later, he showed only precipitins against *P. notatum*. BAL study demonstrated a pattern similar to the previous control (Table 1). The patient changed employment and never again complained of HP symptoms.

■ *Case 2* was that of a 41-year-old man, an ex-smoker, who had worked since 1979 as a driver

and warehouseman for a company that processes and sells cheese. He began to complain of fever, dyspnea, and chest tightness several hours after unloading mold-covered cheese. At our examination, 6 years after onset of symptoms, the patient was asymptomatic; chest radiograph, spirometry, and diffusion capacity were normal, but arterial blood gas analysis revealed slight hypoxemia. The skin prick tests were negative. Precipitins against *P. notatum*, *P. viridicatum*, and *P. brevicompactum* were found. The analysis of the BAL fluid showed alveolitis with marked lymphocytosis, reversal of CD4/CD8 ratio, and increased NK cells (Table 1). Transbronchial biopsy demonstrated pulmonary interstitial sclerosis. He was discharged with the diagnosis of HP. For the next 2 years, he continued to work wearing a mask, but he still had three acute episodes of HP. After changing his occupation, he never again complained of HP symptoms. Repeated BAL analysis showed progressive normalization of total cell count, lymphocyte percentage, and CD4/CD8 ratio.

■ Cheese washing consists of the spreading of coarse salt on the cheese and then rubbing with a wet rag, releasing large numbers of the spores of *Penicillium* species, which cause cheese workers' HP. Its clinical features and BAL cytologic and immunologic features are identical to other forms of HP, thus confirming that these manifestations belong to

Table 1. Bronchoalveolar lavage fluid analysis and serum precipitins at follow-up

Case no. 1	Exposed				
	1987	1989			
Follow-up					
Cells/ml × 10 ³	480	520			
Lymphocytes (%)	68	73			
CD4/CD8 ratio	0.3	0.2			
NK cells (%)	51	27			
Serum precipitins	+	+			
Case no. 2	Exposed		After removal from exposure		
	1985	1987	1988	1990	1994
Follow-up					
Cells/ml × 10 ³	350	220	200	100	80
Lymphocytes (%)	72	69	20	7	11
CD4/CD8 ratio	0.2	0.13	0.52	0.54	0.97
NK cells (%)	18	16	29	14	ND
Serum precipitins	+	+	+	UD	UD

ND = not detected; UD = undetectable.

the HP family. Chest radiography as well as spirometric values may be completely negative some time after the acute episode. As demonstrated by our case no. 2, a careful assessment of exposure to HP antigens is always necessary in suspected cases. The recognition of previous episodes of HP is important for preventive purposes, even if the acute disease is already completely resolved. BAL fluid analysis, as several studies have clearly shown (3, 4), can confirm the diagnosis when the chest roentgenogram is negative. The BAL impairment persists for a long time (5); increased cellularity and lymphocytosis gradually normalize after the end of exposure, whereas reversal of the CD4/CD8 ratio persists for more than 6 years. This study suggests that the BAL analysis may be useful in monitoring inflammatory alveolitis also after the end of exposure.

Key words: bronchoalveolar lavage; cheese workers; extrinsic allergic alveolitis; hypersensitivity pneumonitis; occupational diseases.

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Accepted for publication 11 July 1996

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ALLERGY 1996;51:958-959

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Occupational asthma in a cheese worker

ENZYMES can act as potent occupational allergens. We here report a cheese worker with asthma elicited by work exposure to both pepsin and lysozyme.

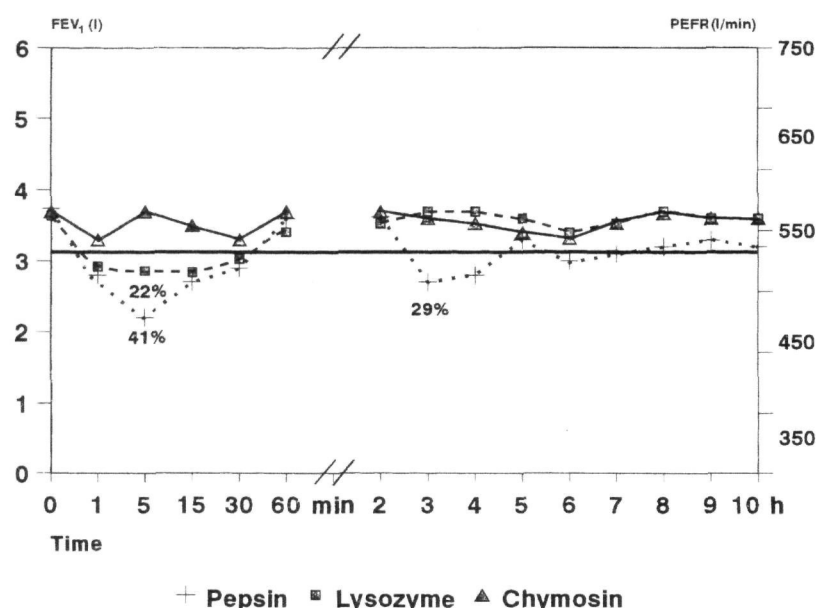


FIGURE 1 Results of inhalation challenge tests.

The patient, a 39-year-old, nonatopic man, had worked in a cheese factory for 11 years, initially in the storage section; however, in the last 3 years, he was directly involved in the production of cheese with cow's milk, milk serum, liquid calcium, rennet powder (50% pepsin and 50% chymosin), and antibutyric enzyme powder (100% lysozyme from egg white). During the last 2 years, he suffered from sneezing, nasal and ocular itching, rhinorrhea, watery eyes, cough, wheezing, and dyspnea. These symptoms developed a few minutes after he started work and persisted for several days. He usually improved on weekends, and became asymptomatic during longer absences.

An IgE-mediated allergy to inhaled pepsin and lysozyme.

The patient was first observed during an asymptomatic period. Physical examination, chest radiographs, and basal spirometry were normal. The bronchoprovocation test with methacholine was positive (PD_{20} - FEV_1 =43 breath units). Skin prick tests with aeroallergens (mites, storage mites, pollens, animal danders, and molds) and foods (cow's milk and hen's egg proteins) were all negative. Total IgE was 27.2 kU/l.

Suspecting occupational disease, we initiated an etiologic study with our patient's informed consent. There were no significant daily fluctuations in PEFR monitoring during 5 days of absence from work. Thirty minutes after beginning work, the patient developed rhinoconjunctivitis, cough, dyspnea, and a 37% fall in basal PEFR.

Skin tests were performed by the prick method with all products that the patient used at work. Cow's milk, liquid ferment, and calcium with the native substance elicited negative results. An immediate wheal 12 mm in diameter was observed with

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