

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.

G. MARCER*, M. FRANCHINI, C. GEMIGNANI, A. ZANCANARO, G. SEMENZATO, C. TASSINARI, A. CIPRIANI, G. FESTI, B. SAIA

*Istituto di Medicina del Lavoro

Via Facciolati 71-35127 Padova

Italy

Tel. +39 49 8216606

Fax: +39 49 8216621

Accepted for publication 11 July 1996

Copyright © Munksgaard 1996

ALLERGY 1996;51:958-959

REFERENCES

1. de Weck AL, Guterson J, Bütikofer E. La maladie des laveurs de fromage ("Käsewascherkrankheit"): une forme particulière du syndrome du poumon du fermier. *Schweiz Med Wochenschr* 1969;99:872-6.
2. Molina C, Aïache JM, Tourreau A, Jeanneret A. Enquête épidémiologique et immunologique chez les fromagers. *Rev Fr Allergol* 1975;15:89-91.
3. Semenzato G, Bjerner L, Costabel U, Haslam PL, Olivieri D, Trentin L. Clinical role of bronchoalveolar lavage in extrinsic allergic alveolitis. *Eur Respir Rev* 1992;2:69-74.
4. Reynolds HY, Fulmer JD, Kazmierowski JA, Roberts WC, Frank MM, Crystal RG. Analysis of cellular and protein content of bronchoalveolar lavage fluid from patient with idiopathic pulmonary fibrosis and chronic hypersensitivity pneumonitis. *J Clin Invest* 1977;59:165-75.
5. Trentin L, Marcer G, Chilosi M, et al. Longitudinal study of alveolitis in hypersensitivity pneumonitis patients: an immunologic evaluation. *J Allergy Clin Immunol* 1988;82:577-85.

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.

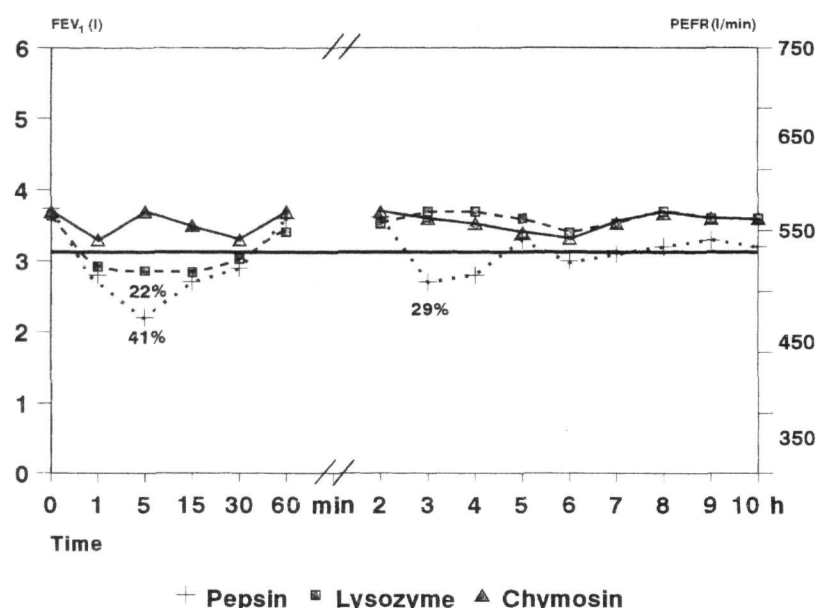


FIGURE 1 Results of inhalation challenge tests.

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

egg lysozyme (100 mg/ml), and of 10 mm with pepsin (1 mg/ml). Chymosin (100 mg/ml) gave negative results. The same tests carried out in three atopic and two healthy volunteers were all negative.

Specific inhalation challenges were performed by the procedure of Pepys & Hutchcroft (1) for dry powder. Pure egg-lysozyme, pepsin, and chymosin powders were single-blind-tested on separate days with a 1-week interval between tests (Fig. 1). There was no significant change in FEV₁ during the challenge with chymosin. After egg-lysozyme inhalation, the patient developed rhinoconjunctivitis, shortness of breath, and a 22% drop from baseline FEV₁; no late response was observed. One minute after pepsin exposure, the patient developed rhinoconjunctivitis, cough, dyspnea, wheezing, dysphonia, and glottic edema, and a 41% drop from baseline FEV₁ was registered. Treatment was administered and the immediate reaction subsided; however, 3 h later, a 29% drop from baseline PEFR was observed. Two nonexposed asthmatics did not experience significant changes from baseline FEV₁ after similar challenge tests.

The assay for IgE-specific antibodies by RAST (2) to lysozyme was positive (12.5 PRU/ml), while showing a negative result to chymosin and pepsin. Specific IgE bound to egg white, egg yolk, ovomucoid, and ovalbumin were undetectable. IgE RAST inhibition (2) of lysozyme RAST by lysozyme was 100%; no inhibition by pepsin or chymosin was observed.

We report the first case of IgE-mediated, occupational respiratory disease caused by both pepsin and lysozyme in a cheese worker. The patient had no previous atopic disorders, and no sensitization to common aeroallergens was demonstrated. The most common cause of respiratory disease in cheese workers, a chronic form of hypersensitivity pneumonitis induced by *Penicillium*, was excluded in our patient.

The patient's clinical history strongly suggested occupational asthma. PEFR monitoring confirmed the work relationship. Specific inhalation challenges identified pepsin and lysozyme as the etiologic agents. The prick tests and RAST results were consistent with a classic IgE-mediated reaction to pepsin and lysozyme. However, the selectivity of the inhibition tests provides clear additional support for the presence of IgE antibodies with lysozyme specificity as well as the absence of cross-reactivity among lysozyme, pepsin, and chymosin.

In the cheese industry, the use of enzymes is common. Carbohydrate-cleaving enzymes (lysozyme) are used as a preservative, and pepsin, like chymosin, is a proteolytic enzyme used as rennet.

Recently, Cartier et al. (2) described the only reported case of a reaction to pepsin powder; this

patient also developed a severe, dual asthmatic IgE-mediated response with the inhalation challenge. Bernstein et al. (3) reported the first well-documented case of IgE-mediated occupational asthma induced by lysozyme. Lysozyme has been considered of little significance as an allergen (4) because of its thermolability, but the presence of specific IgE antibodies to lysozyme is common in egg-processing workers (5, 6).

To our knowledge, this is the first reported case of occupational asthma induced by enzymes (pepsin and lysozyme) in a cheese worker, and also the first reported case of inhalatory sensitization to lysozyme without associated prior egg allergy. We conclude that cheese workers should be considered another group at risk of developing occupational disease due to enzyme allergy.

Key words: occupational asthma; lysozyme; pepsin.

B. AÑIBARRO BAUSELA*, J. L. FONTELA

*C/Arzobispo Morcillo 42 9C

28029 Madrid

Spain

Accepted for publication 2 August 1996

Copyright © Munksgaard 1996

ALLERGY 1996;51:959-960

ACKNOWLEDGMENT

We thank Ifidesa-Aristegui Laboratory (Bilbao, Spain) for performing the immunologic studies.

REFERENCES

1. Pepys J, Hutchcroft J. Bronchial provocation tests in etiologic diagnosis and analysis of asthma. *Am Rev Respir Dis* 1975;112:829-59.
2. Cartier A, Malo JL, Pineau L, Dolovich J. Occupational asthma due to pepsin. *J Allergy Clin Immunol* 1984;73:574-7.
3. Bernstein JA, Kraut A, Bernstein DI, et al. Occupational asthma induced by inhaled egg lysozyme. *Chest* 1993;103:532-5.
4. Hoffman DR. Immunochemical identification of the allergens in egg white. *J Allergy Clin Immunol* 1983;71:481-6.
5. Smith AB, Bernstein DI, London MA, et al. Evaluation of occupational asthma from airborne egg protein exposure in multiple settings. *Chest* 1990;98:398-404.
6. Bernstein DI, Smith AB, Moller DR, et al. Clinical and immunologic studies among egg-processing workers in occupational asthma. *J Allergy Clin Immunol* 1987;80:791-7.

Selective immediate allergic response to penicillin V

ALTHOUGH IgE antibodies often recognize the benzylpenicilloyl (BPO) structure in subjects with immediate allergic reactions to penicillins (1), specific reactions to amoxicillin (AX) (2, 3) and other penicillins (4, 5) have been reported in the last few years, leading to our interest in determining whether selectivity in the allergic response to other β -lactams exists.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.