

Occupational Sensitization to Lactase

D.C.F. Muir, MD,^{1*} A.B. Verrall, RN,¹ J.A. Julian, MMATH,¹ J.M. Millman, MD,²
M.A. Beaudin, RN,² and J. Dolovich, MD¹

Occupational sensitization to lactase is reported in workers formulating and packaging this consumer product, which is used for the relief of gastrointestinal symptoms caused by intolerance to lactose. Allergic rhinitis, conjunctivitis, and some cases of asthma were noted. There was suggestive evidence that atopic individuals may be at greater risk of sensitization. Lactase should be added to the list of potential occupational respiratory sensitizers. Am. J. Ind. Med. 31:570-571, 1997. © 1997 Wiley-Liss, Inc.

KEY WORDS: occupational asthma; enzyme sensitivity; lactase

INTRODUCTION

Lactase is a component of several consumer products and is widely used for the relief of gastrointestinal symptoms caused by intolerance to lactose contained in milk. This disaccharidase enzyme is produced by fermentation, using an *Aspergillus* species. We report an episode of sensitization that occurred in workers formulating and packing the finished product.

MATERIALS AND METHODS

Advice was sought from a plant where respiratory symptoms of allergic rhinitis or asthma were noted in workers shortly after the introduction of the lactase product. The plant was engaged in formulating and packaging a wide range of consumer products for the pharmaceuticals industry. No previous health problems had been noted. As soon as the possibility of sensitization to lactase was recognized, stringent industrial hygiene control was instituted to limit exposure levels. Any individuals with symptoms suggesting possible sensitization were relocated to another worksite. These measures were effective and further cases of sensitization were prevented.

A formal epidemiological study could not be carried out, but all available information was collated to contribute to an understanding of the nature of this episode. Skin prick testing

[Pepys, 1975] was undertaken on as many workers as possible on a voluntary basis, and the majority were so tested. Solutions of lactase enzyme raw material were prepared in concentrations of 0.1, 1.0, and 5.0 mg/dl. Control solutions of histamine and saline were used in a standard fashion. The size of the resulting wheal was recorded and the pattern of results were classified by one of us (J.D.) as positive, negative, or doubtful. A positive result was identified as the presence of a wheal of increasing size according to the concentration of enzyme but with no response to saline. Doubtful responses included obvious dermatographia or instances in which a positive test was observed at one concentration of lactase but was negative at the higher concentrations. These classifications were carried out without knowledge of the clinical status of the individual.

Skin testing to 13 general airborne environmental sensitizers (Bencard), including *Aspergillus*, was carried out on as many individuals as possible. The purpose of this was to identify individuals with an atopic background. The skin test reactions to these sensitizers was classified as positive or negative [Pepys, 1994], and the number of positive reactions provided an index of the degree of individual atopy. Employees with major symptoms of asthma or allergic rhinitis were referred to one of us (D.C.F.M.) for formal diagnosis and clinical management.

A medical chart review of records held by the company was undertaken to identify likely instances of occupational sensitization in workers seen in the medical department of the company either because of symptoms or for purposes of annual health reviews. This medical chart review was carried out without knowledge of the skin test results. Identification criteria included relevant reported symptoms and their temporal relation to work. For each worker, a qualitative estimate of exposure was attempted taking into account such factors as job site, proximity to the lactase operation and duration of employment in that area.

¹Occupational Health Program, Faculty of Health Sciences McMaster University, Health Sciences Centre, Hamilton, ONT, Canada.

²McNeil Consumer Products Co., Guelph, ONT, Canada.

*Correspondence to: Dr. D.C.F. Muir, Occupational Health Program, Faculty of Health Sciences, McMaster University, Health Sciences Centre, Room 3H50, 1200 Main Street West, Hamilton, ONT L8N 3Z5, Canada.

TABLE I. Distribution of Lactase Skin Test Results and Symptoms

Symptom	Lactase skin test result			n	$\chi^2_{(2)\text{association}}$
	–	+	Doubtful		
Eye	6 4.7%	11 16.9%	1 6.7%	18 8.7%	8.1 $p = 0.017$
Nose	12 9.5%	17 26.2%	4 26.7%	33 15.9%	10.3 $p = 0.006$
Respiratory	9 7.1%	9 13.9%	2 13.3%	20 9.7%	2.5 $p = 0.286$
All subjects	127 100%	65 100%	15 100%		

RESULTS

From a total workforce of 279, skin tests to lactase product were carried out on 207 volunteers, 65 were classified as positive, 127 as negative, and 15 doubtful. The medical charts of 210 workers were reviewed; 21 subjects were referred for clinical assessment (D.C.F.M.) either because of severe symptoms or on specific request by the worker; 9 subjects were assessed clinically as having probably occupational asthma; and a further 11 subjects were assessed as having mild symptoms suggesting occupational asthma on the chart review alone. Clinical confirmation of the etiological diagnosis was difficult. This was because of the prompt and permanent removal of these individuals from areas where lactase was in use. The patients were often seen some weeks after last exposure and were usually on treatment with inhaled steroids. Although increased bronchial reactivity was confirmed by a methacholine inhalation test [Hargreave et al., 1985], a specific lactase inhalation challenge was not available. The etiological diagnosis was based only on the reported clinical history and its temporal relation to exposure. The lactase skin test results correlated with nasal ($p = 0.006$) and eye ($p = 0.017$) symptoms, but not with symptoms suggestive of asthma ($p = 0.286$) (Table I). Some individuals had multiple symptoms with streaming eyes, running nose, and tightness of the chest on exposure to lactase powder. There appeared to be no correlation between dermal reactivity and lactase with estimated level of exposure. Of 84 individuals tested for sensitivity to lactase and to the general environmental sensitizers, there was evidence that atopic individuals were more likely to become sensitized to lactase ($\chi^2_{(2)} = 13.409$, $p = 0.001$) and that those with a high degree of atopy, based on the number of positive reactions, were increasingly likely to be sensitized to lactase (χ^2 trend₍₁₎ = 12.880, $p < 0.001$). There was also a positive correlation between those reacting to the lactase test solutions and to the *Aspergillus* test solution ($\chi^2_{(1)} = 6.462$, $p = 0.011$).

DISCUSSION

The investigation was carried out under rapidly changing conditions. Within 6 weeks of starting production, workers with symptoms were identified. Dust levels were very quickly

controlled, and individuals with possible allergic symptoms were removed from any exposure. The episode occurred during the summer months, when symptoms of allergic rhinitis due to environmental sensitizers are common. Not all workers volunteered for investigation or for clinical examination, and there may have been a biased selection of subjects who had allergic rhinitis of nonoccupational etiology.

The lactase solution used for skin testing was obtained from the product in use in the plant. The material is complex and is derived from a fermentation process using a species of *Aspergillus*. About 70% consists of lactase enzyme, and the remainder is of unidentified material derived from the fermentation process (Millman, personal communication, 1995). Presumably, protein fractions of *Aspergillus* were present. This emphasizes the importance of the finding of a positive correlation between sensitization to *Aspergillus* and to the lactase. However, it is clear that sensitivity to *Aspergillus* could only account for a small proportion of the cases who were positive to the lactase. Of 84 individuals tested to both materials, 42 were lactase positive and, of these, only six were positive to *Aspergillus*. The positive correlation between atopy and lactase sensitivity is not unexpected but it should be noted that atopic individuals may have volunteered preferentially for testing.

Somewhat unexpectedly, there appeared to be no evidence that the likelihood of sensitization could be predicted from job site or estimated exposure level. This may be due to the wide dissemination of the fine powder in the ventilation system of the plant, which is of modern design and is of the closed environment type.

After the rapid introduction of strict dust control and, eventually, the elimination of the product, together with rigorous site decontamination, no new cases of sensitization have been noted. Those who appeared to be sensitized have returned to their former work and their symptoms have abated.

There were difficulties in sorting out which workers had symptoms specifically caused by exposure to lactase, as most symptoms were fairly mild (rhinitis and conjunctivitis) in a small community of workers during the summer months, when nonoccupational allergic disorders are common. The strenuous measures taken to reduce and, eventually, to eliminate exposure were clearly effective and the problem was resolved. The evidence suggests that lactase was responsible for the episode. The remedial action taken in the plant was so thorough and so rapid that formal epidemiological proof of the cause of respiratory sensitization was not obtained. However, we obtained unequivocal evidence of skin sensitization to lactase and circumstantial evidence that it probably caused allergic rhinitis and asthma. This material should be added to the list of potential occupational sensitizers so that similar episodes in other plants where production is continuing can be prevented.

REFERENCES

- Hargreave FE, Sterk PJ, Ramsdale EH, Dolovich J, Zamel N (1985): Inhalation challenge tests and airway responsiveness in man. *Chest* 87:S202–206.
- Pepys J (1975): Skin testing. *Br J Hosp Med* 14:412–417.
- Pepys J (1994): Atopy: A study in definition. *Allergy* 49:397–399.