

Detergent Enzymes and Occupational Safety

Observations on Sensitization during Esperase® Production

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During a 10-year survey of 667 workers producing the detergent enzyme Esperase®, derived from an alkalophilic strain of *Bacillus licheniformis*, 31 were found to have been sensitized. All but one were at the same time sensitized to subtilisins, with which they also had been working. No distinction could be made between symptoms attributed to Esperase and symptoms attributed to enzymes derived from *Bacillus subtilis* (*licheniformis*) or other enzymes. Symptoms, when present, were mainly from the lower respiratory tract. Nine sensitized workers were symptom-free. Sensitization was by IgE antibodies and detected by the RAST test. Twenty-one sensitized workers were transferred for precautionary measures or left the company. All 26 sensitized workers, whom it was possible to follow and reinvestigate, were no longer RAST-positive. Ten workers remained in their jobs. No signs of deteriorating lung function or permanent lung damage were found. The study indicated that, when strictly enforced, recommended operating procedures for workers handling hitherto well-known detergent enzymes are sufficient for dealing with Esperase. The data suggest there is no significant risk of consumer sensitization.

Key words: detergents; occupational safety; proteolytic enzymes; sensitization.

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Proteolytic enzymes have been incorporated in laundry detergents since 1963 and widely used since 1968. Until now the main sources of these enzymes have been derived from naturally occurring, non-pathogenic *Bacillus subtilis* (*licheniformis*). The safety in handling these enzymes, which may cause pathological reactions from the respiratory tract and skin (1, 2, 3, 7, 10, 11, 14), was debated at a symposium held in 1976 (5), which concluded that the early detection and publishing on the hazard led to rapid and effective collaborative efforts to identify the nature of the problem and bring it under control. It was also concluded that the enzymes may produce an IgE-mediated asthma or rhinitis, which is dose related, and that exposure levels during manufacture could now be kept so low, that only few would be sensitized.

Occasional cases of sensitization were, however, to be expected to occur. This could be due to a combination of circumstances such as accidental spillage and highly susceptible subjects.

The data from the symposium (5) together with reports on long-term observations from factories which produce enzymes (14), or incorporate these in detergents (8), indicate that respiratory disease other than asthma or rhinitis is unlikely to arise, and that the risk of respiratory sensitization to the enzymatic detergents during their domestic use is extremely small (16). The same data indicated the absence of any average deterioration of lung function related to exposure to detergent enzymes in large groups.

Since 1970 another enzyme belonging to an alkalophilic strain of *Bacillus licheniformis* (6)

has been produced and incorporated in detergents. The enzyme is manufactured under the trade name of Esperase. This paper reports on medical experience accumulated during 10 years of Esperase production.

MATERIAL AND METHODS

All workers engaged in Esperase production have been examined by their company physicians during the observation period November 1970 to November 1980. The total worker population exposed to Esperase dust or aerosol during this period amounted to 667 persons. The workers took part in between one and 15 medical examinations. Between 78 and 348 workers were included in the yearly RAST test investigations. Within the same period all workers were exposed not only to Esperase but also to other enzyme preparations produced by the same company, mainly Alcalase®, a preparation derived from Subtilisin-A.

Blood samples were obtained once a year from all workers exposed to the enzyme and investigated for specific IgE antibodies to Esperase as well as to Alcalase by the RAST test (13). This *in vitro* testing was performed by one of us (L.W.). All workers also had a careful medical history taken and were examined primarily twice a year, later once a year. The medical examination included a lung function test (FEV₁). The workers have also had several chest X-rays taken during the observation period.

An extensive study on the worker population covering the years 1970 to 1972 has been published (14) and the prolonged observations throughout 1975 were presented at the above mentioned symposium (5), this total investigation included 830 workers. Both studies, however, were primarily related to Alcalase. The present investigation reports on sensitization to Esperase.

RESULTS

Table 1 shows that during the period 1970 to 1980 a total of 31 workers (4.6%) were sensitized to Esperase according to RAST test. All but one worker were also sensitized to Alcalase.

Table 1
Numbers of workers newly sensitized to Esperase during the years 1970 through 1980. Sensitization was determined by the RAST test

Year	No. of sensitized workers
1970	3
1971	5
1972	2
1973	8
1974	9
1975	0
1976	3
1977	0
1978	0
1979	1
1980	0
Total	31

Table 2
Respiratory tract symptoms in 31 workers sensitized to Esperase. All workers but one were also sensitized to Alcalase

Symptoms	No. of workers
Nasal and throat irritation or rhinitis	6
Frequent coughing alone	2
Shortness of breath and chest tightness	16
No respiratory tract symptoms	9

Table 3
General rules for transfer of enzyme workers

Reason	Procedure
Severe symptoms + positive RAST	removal to non-enzyme work
Milder symptoms + positive RAST	removal to non-dusty enzyme work or non-enzyme work
No symptoms + positive RAST	careful observance but no removal
Symptoms and negative RAST	according to findings

The total number of Alcalase-sensitized workers during the same period was 70.

Not all Esperase-sensitized individuals had symptoms (Table 2). Little more than half of the sensitized workers had occasional complaints of frequent coughing, shortness of breath or tightness of the chest. Normally, no distinction could be made between symptoms attributed to Esperase and symptoms attributed to Alcalase or other enzymes. No permanent deterioration of lung function was observed. No pathological findings, which could be related to enzyme exposure, could be seen on the roentgenograms.

Of the sensitized workers, 21 were transferred either to non-dusty enzyme departments or to non-enzyme departments, or left the company. Ten workers remained in their jobs and became no longer RAST-positive. The general rules for transfer appear in Table 3. The safety measures taken have been in general agreement with the recommendations issued by the S.D.I.A.* for operating procedures in U.K. factories handling enzyme materials (12). RAST tests, however, have been the normal way of monitoring the sensitization rate to enzymes, while skin tests have been used either to confirm a positive RAST or in order to receive immediate information in a clinical situation.

Twenty-six workers, including two who had left the company, were reinvestigated and all found to be no longer RAST positive. In several cases workers converted from RAST-positive against Esperase to RAST-negative within 1 year, i.e. at the next examination. Four workers were not reinvestigated as the company physicians were unable to locate them, and one patient had died.

Skin problems, which in the early days of enzyme production seemed to be a major problem (10, 15), became within the observation period almost negligible, and all were found within the pattern previously reported (15).

COMMENTS

Our results show that similar to workers exposed to subtilisins (5, 8, 14), workers exposed to the detergent enzyme Esperase may be sensi-

tized and that some of the sensitized individuals may develop an IgE-mediated asthma or rhinitis. It is of importance to note that among Esperase workers no clinical symptoms were found that have not already been known to occur in workers exposed to subtilisins (5).

The precautions generally agreed upon in order to minimize sensitization (4, 12) seem to have been sufficient for reducing the sensitization rate. The precautions include training and supervision of personnel handling enzymes, improvements in local exhaust ventilation and personal protection, constant monitoring of dust levels, care in handling discarded garments of workers, and enforcement of rules concerning handling of waste and spillage. One of the important measures undertaken at the enzyme factories has been a careful preemployment investigation of prospective employees and exclusion of persons suffering from chronic lung diseases or atopic diseases from working within areas of exposure to enzyme dust or aerosols (14). Atopics are more likely to develop sensitization to proteolytic enzymes than non-atopics (5, 8, 14).

Although the present study does not include individuals in contact with detergents but only with enzymes, the data showing a conversion from RAST-positive to RAST-negative even in workers still employed in Esperase production make it unlikely that there is any significant risk of sensitization during domestic use of the enzyme. Workers in enzyme production cannot be totally protected against enzyme dust or aerosol, and are operating in an enzyme-contaminated environment during full working hours, whereas housewives today are exposed primarily to encapsulated enzymes (9), and only for minimal periods of time.

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