

OCCUPATIONAL ENZYME DERMATITIS

Results of Patch Testing with Alcalase®

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Abstract. 79 workers from two detergent-enzyme producing factories and twelve controls were submitted to patch testing with the proteolytic enzyme alcalase. None showed allergic patch test reactions. Higher concentrations of enzyme produced primary irritant reactions in patch tests in both workers and controls. The symptoms of occupational dermatitis are described. It is concluded that occupational enzyme dermatitis is of a primary irritant nature. The results of the study indicate that it is unlikely that conventional use of biological detergents containing alcalase will be attended by hazards of cutaneous sensitization.

Proteolytic enzymes from *Bacillus subtilis* (subtilisins) have been in use for laundry detergents for almost a decade. Two types of subtilisins exist, subtilisin A and B. Alcalase® (Novo Industri A/S, Copenhagen, Denmark) is a commercial enzyme preparation derived from subtilisin B. The action of the subtilisins which hydrolyse most common proteins is relatively non-specific. Although the enzymes act more readily on denaturated protein, native protein too is attacked to a certain degree (11). Both subtilisins have been reported to have induced respiratory tract illness and injury to the skin among workers in plants that manufacture enzymes or enzyme-detergent products (6, 7, 12, 13, 14), while illness due to detergent enzymes among consumers of laundry products seems extremely rare.

Whereas enzyme-provoked respiratory symptoms may be due to allergy (6, 7, 14), it is generally assumed that most skin symptoms are primary irritant reactions (7). However, in spite of this assumption, no larger series of patch testing have been reported in the literature. This paper reports on patch testing in patients with occupa-

tional enzyme dermatitis as well as in a small number of non-enzyme exposed controls.

MATERIAL AND METHODS

These studies were carried out at two factories where alcalase is produced (Novo Enzyme Factories in Copenhagen and Kalundborg). More than 400 workers have been engaged in enzyme production in these two factories. In initial studies, 12 persons without previous contact with alcalase or other detergent enzymes and 18 workers with occupational dermatitis due to alcalase were exposed to patch tests with alcalase in aqueous solution for 48 hours. The tests were carried out in accordance with Blohm's method (3). The concentration of the test samples was 0.01%, 0.1% and 0.5%. Later, a further 61 workers, who had experienced subjective and objective skin symptoms during production, were tested with 0.01% alcalase.

RESULTS

Table I shows the results of the initial studies. Four controls and 2 workers showed an erythematous irritant reaction to patch tests with

Table I. *Primary irritant reactions in patch tests in workers with occupational alcalase dermatitis and non-alcalase exposed controls*

	No. of persons	No. of reactors		
		Alcalase 0.5 %	Alcalase 0.1 %	Alcalase 0.01 %
Workers	18 ^a	2	1	0
Controls	12	4	0	0

^a Further 61 workers showed negative reactions to alcalase 0.01%.



Fig. 1. Primary irritant dermatitis of hands of an alcalase worker showing typical erosions on the volar surfaces of the fingertips.

0.5% alcalase. One worker showed a similar reaction to alcalase 0.1%. The erythematous reaction was typical of a mild reaction to primary irritants (2). None among the initially tested showed positive reactions to alcalase 0.01%, the concentration chosen for subsequent testing. No patients and no controls showed responses typical of allergic contact dermatitis.

None of sixty-one workers studied later showed positive reactions. These workers as well as the 18 initially tested all had experienced either burning or itching of the skin and all had exhibited objective skin symptoms. The lesions were in most cases restricted to the hands, forearms and face. Other areas affected were the armpits and groins, all perspiring parts of the body. Occasionally, more pronounced reactions were found. These consisted of erosions (Fig. 1) or pustules (Fig. 2) localized to the volar surfaces of the fingertips. In almost all cases a marked local hyperhidrosis of the palms or fingers was observed. Milder dermatitis disappeared during week-ends. Regularly the dermatitis disappeared during vacation. In only a few persons did the dermatitis result in absence from work. In one case it was found necessary to transfer a worker to a none-enzyme department in the same factory. In all cases the enzyme dermatitis responded well to treatment with topical steroids and local potassium permanganate baths. Following intensified prophylac-

tic measures in the form of more frequent change of working clothes, prophylactic skin care, use of protective gloves and masks, and powdering in order to keep the skin dry, the frequency of dermatitis decreased rapidly. While 43% of workers in the enzyme factories complained of skin symptoms during the first year of large scale production, only 21% complained 2 years later.

DISCUSSION

Enzyme dermatitis is an occupational, not a consumers dermatitis. Skin symptoms, such as those reported in this study, have not been seen among users of enzyme detergents attending our two outpatient clinics. Whereas a similar type of dermatitis has been described in workers occupied with dry concentrated extracts of pancreas (4). The visible skin signs are caused by exposure to high concentrations of enzyme.

Isolated reports on enzyme dermatitis among consumers have been reported in the literature (1, 5, 8, 15, 16). However, in none of these cases can it be said that the cause of the dermatitis was definitely established. In most cases patch tests with pure enzyme preparations were not performed, or were carried out with concentrations (16) which in our hands caused primary irritant reactions. A phototoxic or photoallergic reaction

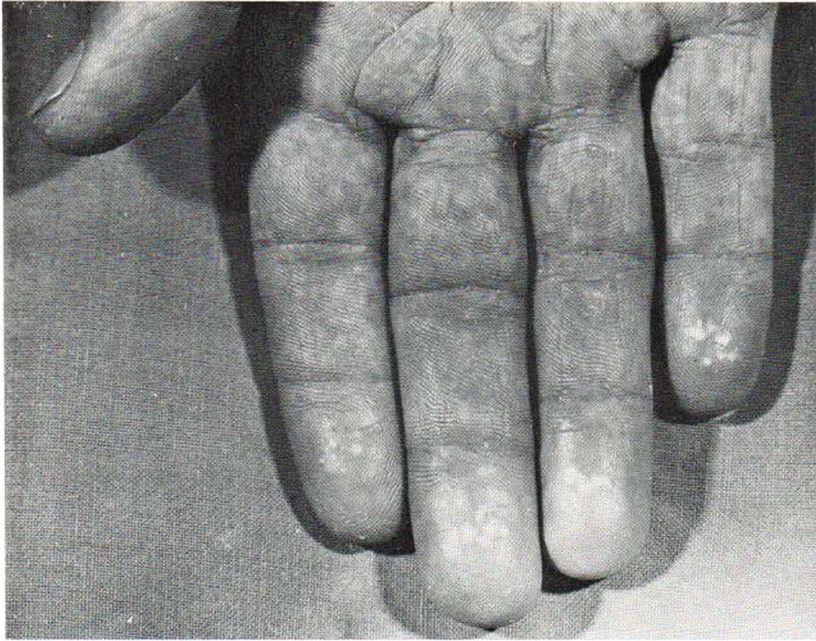


Fig. 2. Pustules on volar surfaces of fingertips in primary irritant enzyme dermatitis.

to proteolytic enzymes as suggested by Jensen (8) has never been established, and phototoxic and photoallergic reactions have not been observed among the more than 400 enzyme workers from the two alcalase-producing factories included in our study.

The nature of the primary irritant dermatitis is not fully understood. Proteolytic enzymes usually break down denaturated protein much faster than native protein, possibly due to the effect of inhibitors located in the cells. It appears, however, that microbial proteinases are not inactivated by inhibitors to the same extent. Plasma kinins, believed to be mediators of inflammatory reactions, may also contribute to the formation of an alcalase dermatitis. Kinin-forming enzymes are activated *in vitro* by alcalase (9).

The enzyme dermatitis cannot be considered a great hazard to workers because most reactions are mild and of transient nature. Prophylactic measures, however, may greatly diminish the inconveniences. The reduction in skin symptoms among workers exposed to alcalase, reported here, is no doubt due to prophylaxis. It seems of specially great importance to keep the skin dry. When enzymes are not in solution, they do not function.

The absence of allergic patch test reactions among workers with enzyme dermatitis confirm

the conclusions from predictive patch testing with alcalase (10), that the potentiality of this enzyme to induce contact allergy is extremely low. The results of this study indicate that it is unlikely that conventional use of enzyme detergents will be attended by hazards of cutaneous sensitization.

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