

## Short Communication

### Occupational contact urticaria from cellulase enzyme

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#### Case Report

A 38-year-old process man had worked in the same factory for 14 years, mainly on the distillation of ethanol. He had some atopic and work-related rhinitis, but when he started to work in the production of starch from barley, he developed within some months more severe rhinitis, pruritus and mild whealing on his upper arms when exposed to dust at work. Occupationally, he was exposed to both barley and oat dust. Furthermore, cellulase enzymes were used in the production of starch. Previously, he had not had atopic or other skin symptoms. Prick tests were performed as described earlier (1) and showed allergic reactions to mugwort pollen (diameter of wheal 5 mm=2+), dog epithelium (5 mm=2+), cat epithelium (6 mm=2+) and *Pityrosporum ovale* (7 mm=3+) (histamine hydrochloride 10 mg/ml; 7 mm=3+). Other skin prick test reactions to environmental allergens, flours, storage mites and molds were negative. He was then investigated for allergy to industrial enzymes.

#### Preparing cellulase for prick testing

A commercial cellulase preparation (Econase CEP®, Alko Ltd, Finland) was used as the test enzyme. Dry

cellulase was extracted in 0.1 M potassium phosphate buffer, pH 7.4, and diluted with Coca solution (0.5% sodium chloride, 0.3% sodium hydrogen carbonate, 0.4% phenol) to achieve a protein concentration of 200 µg/ml. A part of this solution (2.5 ml) was passed through a Millex-GV filter containing a 0.22 µm membrane (Millipore Ltd) into a sterile vial containing 2.5 ml glycerol, to yield a final protein concentration of 100 µg/ml. The Coca-glycerol solution served as a negative control.

#### IgE measurements

Specific IgE antibodies to cellulase were measured by a radioallergosorbent test (RAST). Cellulase was conjugated to cyanogen-bromide-activated paper discs by the method of Ceska et al. (2). Other reagents for RAST were obtained from the Phadebas RAST kits (Pharmacia & Upjohn, Sweden). The results, in kU/l, were based on the RAST reference serum (Pharmacia & Upjohn, Sweden). Values >0.3 kU/l were defined as positive (elevated), and <0.3 kU/l as negative.

The patient's prick test reactions to industrial enzymes are given in Table 1, showing that only cellulase provoked a positive reaction. RAST to cellulase was elevated, 1.5 kU/l. 20 control persons were negative on prick testing with the enzymes.

Table 1. Prick test results with a series of industrial enzymes (0=no wheal)

| Prick test substances; enzymes and controls | Origin of prick test substance | Wheal diameter (mm) |
|---------------------------------------------|--------------------------------|---------------------|
| histamine HCl (10 mg/ml)                    |                                | 7 mm (=3+)          |
| negative control                            |                                | 0                   |
| Coca-glycerol control                       |                                | 0                   |
| cellulase                                   | fungal                         | 5 mm (2+)           |
| xylanase                                    | fungal                         | 0                   |
| glucose-oxidase                             | fungal                         | 0                   |
| pectinase                                   | fungal                         | 0                   |
| protease                                    | bacterial                      | 0                   |
| protease                                    | fungal                         | 0                   |
| α-amylase                                   | bacterial                      | 0                   |
| α-amylase                                   | fungal                         | 0                   |
| α-amylase                                   | bacterial                      | 0                   |
| phytase                                     | fungal                         | 0                   |
| protease                                    | bacterial                      | 0                   |
| lipase                                      | fungal                         | 0                   |

#### Discussion

New methods in biotechnology have led to a rapid increase in industrial-scale production and use of enzymes (3–5). Industrial enzymes may cause allergic symptoms such as asthma (4–7), rhinoconjunctivitis (4–7), pharyngeal edema (8), allergic contact dermatitis (9–11), and contact urticaria (10–13), as in the present case, together with rhinitis from cellulase.

Cellulase is used as an additive in baking, brewing, animal feeds, composting, the textile industry, detergent, starch and sugar production, and in the pulp and paper industry (4, 5, 8). The commercial enzyme preparation is either liquid or dry powder. The use of cellulases and hemicellulases has greatly increased during the past decade (3) and several cases of allergy caused by cellulases have been reported (6, 8, 10, 11). 4 cases of contact urticaria, developing after 0.5–4 years of exposure to the enzymes cellulase and xylanase, were reported by Kaner-

va & Tarvainen (10). All 4 patients later developed rhinitis and asthma, and 2 of them allergic contact dermatitis (11). Skin prick tests and RASTs were positive to cellulase and xylanase in all cases. Contact urticaria was recently reported from phytase (13). Other industrial enzymes that have caused allergic reactions of the skin were recently reviewed by Kanerva & Brisman (5).

A recent study from Finland confirmed that the currently used industrial enzymes are strong sensitizers (13). Sensitization may follow minute exposure; even office personnel in factories may become sensitized. Proper control of exposure is mandatory (13).

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