extract. There were parallel decreases in the reactions to food allergens derived from banana, kiwi, and chestnut.

Absolute values of IgE to latex showed no significant alterations except at the end of the study, when an increase of approximately 4–6 URAST/ml was seen. However, IgE specific for chestnut clearly decreased during treatment from 0.72 to 0.30 kU/l). The behavior of IgG class specific for latex was similar to that of specific IgE. We did not detect latex-specific IgG4 during the study; however, this immunoglobulin apparently began to appear at the end of the study.

Clinical symptoms improved steadily, with an evident reduction in nasal obstruction and eye manifestations. This was corroborated by the patient, who reported improvement even in areas of the hospital that produced significant exposure to latex gloves, which she had previously been unable to tolerate. Acquisition of tolerance to the environment in her workplace was gradual during SIT, but was more pronounced once the maintenance period was started upon her discharge from the hospital and return to work. Because of the occupational nature of the allergy, the best provocation test for the allergen was constant exposure to latex in the workplace. However, we also used specific, controlled provocation tests. The patient entered a 1-m^3 airtight cabin and handled four pairs of latex gloves for 15 min; her clinical symptoms were then evaluated during the 6 h following this exposure to the allergen. Clinical examination after the provocation test showed that she had no cutaneous, eye, nasal, or bronchial symptoms during the following 6 h.

In terms of local reactions, tolerance of SIT was excellent, with no delayed local reactions and only one episode of immediate local reaction during the maintenance phase (erythema with papules measuring 60 mm in mean diameter). This reaction did not require treatment or a change in the desensitization schedule.

We believe that the allergenic extract is safe, at least at concentrations up to 0.4 μg latex protein. Tolerance was excellent, and, like other authors who used accelerated schedules (6), we established the MD on the basis of the appearance of a systemic reaction. We felt this to be the most prudent approach, in contrast to other studies in which the appearance of a systemic reaction led only to a change in the dose schedule (7, 8). Use of a conventional schedule would probably have allowed us to reach a higher MD, a possibility that deserves further study.

We consider SIT with latex to be highly effective, and found the allergenic extract used to be safe and well tolerated.

*Imuno-Alergologia, Hospitais da Universidade de Coimbra, 3000 Coimbra, Portugal

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Allergen-induced matrix metalloproteinase-9 in nasal lavage fluid

A.W. van Toorenenbergen*, R. Gerth van Wijk, A.M. Vermeulen

Key words: allergic rhinitis; eosinophil cationic protein (ECP); metalloproteinase; MMP-9.

• In an individual with allergic rhinitis, exposure to allergens leads to rapid release of mast-cell-derived mediators. In about half of the subjects, this immediate nasal response is followed 3–12 h later by a late-phase response (1). This secondary response is induced by inflammatory cells, which have accumulated in response to mast-cell-derived chemotactic factors (1). Bronchoalveolar eosinophilia is a hallmark of late-phase IgE-mediated reactions (2). Okada et al. (3) recently showed that matrix metalloproteinase-9 (MMP-9) is required for migration of eosinophils through basement membrane components *in vitro.* Indeed, elevated levels of MMP-9 were recently found in the bronchoalveolar lavage fluid of asthmatics (4).

Nasal provocation with allergen induces a parallel release of ECP and matrix metalloproteinase-9 during the late-phase inflammatory response.

In a previous study (5), we measured albumin, eosinophil cationic protein (ECP), and other mediators in nasal lavage samples obtained before and up to 10 h after nasal allergen provocation. In the present study, we sought for MMP-9 in five series of these nasal lavage samples. Our results show a parallel release of ECP and MMP-9 after nasal provocation with allergen. Allergic rhinitis of the five patients involved in this study was confirmed by positive skin tests to grass pollen and/or house-dust-mite extract. Informed consent was obtained from all patients, and

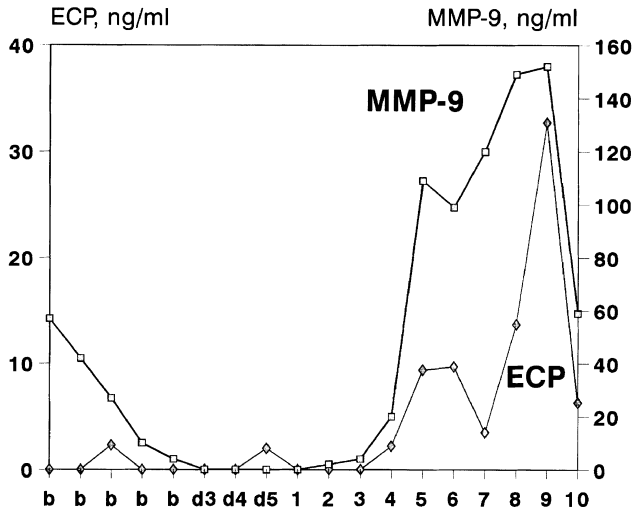

Figure 1. ECP and MMP-9 in nasal lavage fluid after nasal challenge with house-dust-mite extract. b) Lavage before challenge; d3, d4, d5) Lavage after challenge with *D. pteronyssinus* extract (10^3, 10^4, and 10^5 SQU/ml, ALK, Denmark). 1–10) Hours after last allergen challenge.

the study was approved by the medical ethical committee of the University Hospital Rotterdam-Dijkzigt (5).

Before nasal challenge with allergen extract, nasal lavage was performed four times to obtain baseline mediator levels. Nasal lavage was performed as described by Naclerio et al. (1).

Both nostrils were washed with 5 ml saline, prewarmed to 37°C.

To prevent nasal congestion, 0.125 ml 0.1% oxymetazoline was sprayed into each nostril 5 min before the first allergen challenge. For allergen challenge, 0.125 ml allergen extract was sprayed into each nostril, and 10 min later nasal lavage was performed. Lavage fluid was collected in plastic tubes and kept on ice. Within 1 h after collection, the lavage fluid was centrifuged; the supernatant was stored at –20°C.

MMP-9 was determined by ELISA (Biotrak, Amersham, Buckinghamshire, UK) according to the manufacturer's instructions. This ELISA primarily detects proMMP-9 (MMP-9 proenzyme) and proMMP-9 bound to tissue inhibitors of metalloproteinases (TIMPs-1 and -2). ECP was estimated by RIA, according to the manufacturer's instructions (Pharmacia, Uppsala, Sweden).

In four patients, maximum MMP-9 levels were observed 9 or 10 h after nasal provocation with allergen. In Fig. 1, the results of nasal lavage are shown for one of these four patients. In the fifth patient, a maximum MMP-9 level (340 ng MMP-9/ml lavage fluid) was already observed 3 h after allergen provocation. As shown before (5), a maximum ECP level in lavage samples from this patient was also seen as early as 3 h after nasal provocation.

Matrix metalloproteinases, a family of zinc-dependent proteases, have been implicated in pathologic tissue degradation in diseases such as rheumatoid arthritis, osteoarthritis tumor invasion, and, recently, asthma (4). Our results further extend these observations into the field of allergic rhinitis.

The ELISA we used primarily recognizes enzymatically inactive proMMP-9; active MMP-9 has only 2.7% cross-reactivity with proMMP-9 in this ELISA (information supplied with the MMP-9 ELISA, Amersham). The relative amounts of active MMP-9 and proMMP-9 in lavage samples should be the subject of a future study. In summary, our study indicates that nasal allergen provocation induces MMP-9 release as part of the late-phase inflammatory response.

*Department of Clinical Chemistry, University Hospital Rotterdam Dijkzigt, PO Box 2040, 3000 CA Rotterdam, The Netherlands, Fax: +31(0)10 4367894, Email: toorenenbergen@ckcl.azr.nl

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Isoniazid-induced bullous skin reaction

P. Scheid*, G. Kanny, Ph. Tréchot, V. Rosner, O. Ménard, J.M. Vignaud, D. Anthoine, Y. Martinet

Key words: epidermal necrolysis; isoniazid; pemphigoid; tuberculosis.

● Cutaneous eruptions, the most frequent adverse reaction to isoniazid (2% of patients), include acneiform eruption, urticaria, purpura, lupus erythematosus-like syndrome, pellagra-like syndrome, exfoliative dermatitis, toxic