

labelled with horseradish peroxidase (Sigma). Chemiluminescent staining was performed using Westernbreeze (PerBio Science, Aalst, Belgium). The intensity was photographed using a Chemidoc gel documentation system (BioRad Laboratories, Nazareth Eke, Belgium) and analysed with Quantity One software (BioRad). The patient showed an almost fivefold higher intensity for IgE compared with the highest control. IgE staining against *S. cerevisiae* was negative.

Modern rHBV vaccines are manufactured by harvesting hepatitis B surface antigen (HbsAg) from cultures of recombinant strains of *S. cerevisiae* transfected with the HbsAg gene. HBvaxPRO® contains HbsAg that is absorbed to amorphous aluminium-hydroxyphosphatesulphate. Excipients are sodium chloride, sodium borate and water.

Although rHBV vaccines are considered effective and safe drugs (1), different rHBV-vaccine-related adverse events have been identified and published. The cutaneous adverse effects of rHBV comprise local and generalized reactions (2, 3). Local cutaneous events predominantly consist of transient inflammatory reactions resulting from nonspecific lymphoid or granulomatous reactions. Allergic reactions to the vaccine strain, adjuvants, conservatives or other excipients are less frequently involved in local cutaneous adverse reactions and remain anecdotal. Brightman et al. (4) described a comparable case clinic and presumed the reaction to result from an IgE-mediated *S. cerevisiae* allergy.

We present a patient in whom the regional and temporal relationship between injection and symptoms is highly indicative of an rHBV-related adverse event. This presumption is endorsed by the positive basophil activation test (BAT) and IgE-blotting results for the vaccine and the absence of sensitization from alternative causes.

The principals and diagnostic applications of the BAT are discussed elsewhere (5). It emerges that the BAT can also help diagnose allergy from rHBV. Although the BAT does not discriminate between IgE and non-IgE-mediated reactions,

according to the blotting experiments, it appears that the reaction in our patient could be IgE-mediated. This finding that IgE to be involved in the pathomechanism of extensive large local reactions seems similar to the observation in Hymenoptera venom allergy (6). In our opinion, demonstration of an IgE-mediated mechanism seems to preclude re-administration of rHBV in our patient.

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Exhaled breath temperature as a marker of airway remodelling in asthma: a preliminary study

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Key words: airway remodelling; asthma; exhaled breath temperature.

The proliferation of mucosal blood vessels and the deposition of extracellular matrix are considered the main contributors of airway remodelling in asthma (1).

Exhaled breath temperature (EBT) has been reported to be related to the degree of airway inflammation in asthma (2, 3) and it has been hypothesized that its increase could be on account of an increased vascularity of airway wall (2).

Metalloproteinase-9 (MMP-9) is a mediator, which is considered to play a pivotal role in the mechanisms of airway inflammation and remodelling in asthma, being potentially involved in a number of processes regulating connective tissue deposition and degradation (4).

In this pilot study, we aimed to investigate whether the level of EBT can be related to MMP-9 for the purpose of exploring a preliminary hypothesis of a potential application of EBT as a noninvasive marker of airway remodelling in asthmatic children.

Twenty-six house dust mite-sensitized children (8–14 years) with mild-to-moderate asthma were evaluated. Ten of them were receiving inhaled corticosteroids at low dosage (fluticasone propionate ≤ 200 µg/day) and none of them reported re-exacerbation of asthma in the 4 weeks prior to the study. None of them had been receiving oral steroids for at least 3 months prior to the study period.

Exhaled breath temperature could be a marker of airway remodelling in asthma.

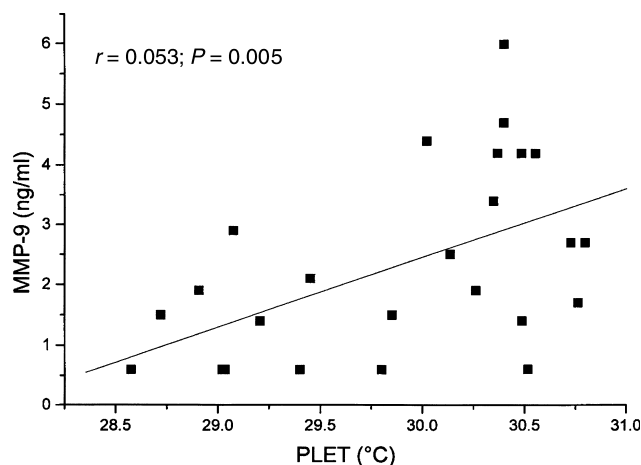


Figure 1. Relationships between end-expiratory manoeuvre plateau temperature and metalloproteinase-9 concentration in sputum supernatant.

The study was performed at the Istituto Pio XII, Misurina, Belluno (Italy) and it was approved by the local ethics committee.

Exhaled breath temperature was evaluated as previously described (3). Briefly, exhaled airway temperature was measured during a maximal slow exhalation with a mouth pressure of > 5 cm H₂O and flow at 5–6 l/min, using the Medical Mass Flow Sensor of the Vmax Spectra 229 Pulmonary Function Laboratory (VIASYS Healthcare, Yorba Linda, CA, USA). Dynamic airway temperature and air flow were sensed from the Mass Flow Sensor. Real-time signal display consisted of inspiratory and expiratory airway temperature, respiratory flow and mouth (airway) pressure on a time axis.

At the end of the test, the software automatically calculated the end-expiratory manoeuvre plateau temperature (PLET) (3).

Sputum was induced in asthmatic children with the inhalation of hypertonic saline solution, using a standardized method (3) and the supernatant was collected for MMP-9 assay.

Metalloproteinase-9 was assayed by enzyme-linked immunosorbent assay (Human Biotrak Assay; Amersham Biosciences, Piscataway, NJ, USA).

Figure 1 shows a scattergram presenting the individual relationships between

PLET and MMP-9, which reveal a statistically significant correlation between the two parameters ($r = 0.53$; $P = 0.005$).

The finding from the present preliminary study suggests that EBT measured at the end-expiratory plateau (PLET) is related to MMP-9, which is considered a relevant marker of airway remodelling in asthma (4).

It is tempting to speculate that a possible explanation for this concordance could be the relationship between remodelling and vascularization of the airway in asthma. A relationship between fibrosis of the bronchial wall and proliferation of blood vessels, in association with increased levels of vascular endothelial growth factor (VEGF) has been demonstrated (5). It has also been reported that the expression of MMP-9 is closely related to the level of VEGF in the sputum from asthmatic patients (6), thus suggesting that VEGF signalling can regulate the expression of MMP-9 playing a critical role in the initiation and maintenance of asthma.

The demonstration that there is a significant relationship between PLET and MMP-9 opens up a new perspective for future studies aimed at assessing a possible role of EBT in detecting and monitoring airway remodelling in asthma.

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