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Absorption across the nasal airway mucosa in house dust mite perennial allergic rhinitis

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Introduction

It has been postulated that increased airway tissue permeability (increased absorption) is critically involved in the development and/or the persistence of allergic airway disease (Leskowitz et al., 1972; Aas, 1978). Airway hyperpermeability is also considered a pathogenic mechanism in established airway inflammation causing non-specific hyper-responsiveness (Hogg, 1981). This attractive hyperpermeability hypothesis may receive some support from previous reports dealing with animal (Boucher et al., 1977; Ranga et al., 1983) and human experiments (Salvaggio et al., 1964; Buckle & Cohen, 1975; Inagaki et al., 1985; Ilowite et al., 1989). However, well controlled human studies involving asthmatic subjects (Elwood et al., 1983; O’Byrne et al., 1984; Halpin et al., 1993) and patients with seasonal allergic rhinitis (Greiff et al., 1993, 1997) have challenged the hyperpermeability hypothesis by demonstrating unchanged or even decreased airway absorption during active disease periods.

The possibility that allergens with enzymatic activity might damage the epithelium and increase airway absorption has received attention (reviewed in Robinson et al., 1997). House dust mite allergens express enzymatic activity (Stewart et al., 1989) and may produce epithelial damage and increased mucosal perviousness in vitro (Herbert et al., 1990, 1995). Although in vitro studies of airway absorption have unknown relevance to the in vivo condition (e.g. epithelial restitution may be prompt in vivo but not in vitro (Persson et al., 1997)) these observations are of interest. For example, the possibility exists that perennial allergic rhinitis, where house dust mite is a major culprit, may exhibit a more deranged absorption barrier than in the seasonal pollinosis where a functionally tight mucosa has been demonstrated (Greiff et al., 1993, 1997). In the present study we have thus examined nasal airway absorption in patients with perennial house dust mite allergic rhinitis compared with healthy subjects.

Materials and methods

Study design

Nasal absorption of desmopressin (1-deamino-8-D-arginine vasopressin) was examined in patients with perennial allergic rhinitis and in healthy subjects. The patients with allergic rhinitis were examined after withdrawal of treatment for 4 weeks when...
symptoms of allergic rhinitis were evident. The healthy subjects were examined together with the patients. The urinary excretion of desmopressin in 24 h urine samples was calculated after its nasal administration as an index of nasal mucosal absorption.

Patients and healthy subjects
Fifteen patients with perennial allergic rhinitis (aged 22–35 years) were enrolled and examined during a period from December to February, i.e. outside the season for, e.g. birch and grass pollen allergy. All patients had a history of perennial house dust mite allergic rhinitis, which was verified by a positive skin prick test (Aquagen SQ, ALK, Copenhagen, Denmark). Eight healthy subjects (aged 22–27 years) participated as controls. These subjects had no history of allergic rhinitis and a negative skin prick test to seasonal and perennial allergens. The study was performed after approval by the local ethics committee and according to the declaration of Helsinki. Informed consent was obtained from the subjects.

Nasal symptoms
On-going medication (in all patients topical glucocorticosteroid treatment) was withdrawn and nasal symptoms were scored for 4 weeks. The patients with allergic rhinitis were instructed to register nasal blockage and discharge on a four graded scale during the treatment withdrawal period. The symptoms were scored as 0: no, 1: mild, 2: moderate, and 3: severe symptoms. Only patients who developed significant nasal symptoms of allergic rhinitis, chosen to be a score of 2 or more of either symptom, were further examined. Accordingly, seven symptomatic patients were subsequently examined with desmopressin nasal absorption measurements.

Nasal administration of desmopressin
Desmopressin (20 µg ml⁻¹) in isotonic saline was administered onto the mucosal surface of the right nasal cavity using a nasal pool-device (Greiff et al., 1990). The device contained 15 ml of the desmopressin (tracer) solution. The solution was maintained in contact with the nasal mucosa for 15 min and subsequently recovered. The mucosal surface was irrigated immediately after the completed tracer instillation in order to prevent uptake of retained tracer beyond the 15 min of exposure. These irrigations were carried out with isotonic saline using two nasal pool-devices, each containing 15 ml fluid. These fluids were maintained in contact with the nasal mucosa for periods of 30 s each.

Monitoring of nasal absorption of desmopressin
Urine was collected for 24 h after the completed nasal administration of desmopressin. The concentration of desmopressin in urine was determined and the total amount excreted during the 24-h period was calculated. The concentration of desmopressin was analysed by a specific radioimmunoassay that previously has been described in detail (Fjellstad-Paulsen et al., 1993). The cross-reactivity with arginine vasopressin and oxytocin was less than 0.01%. The detection limit of desmopressin was 5·0 pm.

Statistics
Mann–Whitney U-test was used for comparisons between absorption level patients with allergic rhinitis and the group of healthy subjects. A P-value <0·05 was considered significant. Data are presented as mean ± SEM.

Results
The amount of desmopressin in urine excreted during the 24-h sampling period did not differ between patients with perennial allergic rhinitis and healthy subjects (P = 0·1) (Fig. 1). There were no significant differences between the urine volumes between these groups being 955 ± 91 ml in healthy subjects and 1211 ± 218 ml in patients with perennial allergic rhinitis (P = 0·1).

Discussion
The present study demonstrated significant nasal absorption of desmopressin in patients with perennial allergic rhinitis. However, the acute absorption capacity of the nasal airway mucosa in these patients did not differ from that recorded in healthy subjects. These results are at variance with the view that an abnormal pervious nasal epithelial lining is an important mechanism in airway disease caused by house dust mite allergens. Displacement of nasal absorption tracers to the gut may interfere with nasal absorption measurements (Greiff et al.,...
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... but this problem may be circumvented by employment of a suitable tracer. Desmopressin is valid as a specific tracer of nasal absorption in this context because the bioavailability after oral administration is low compared with that after nasal administration (Fjellstad-Paulsen et al., 1993). In the present study, particular care was also taken to prevent extranasal distribution of the tracer (by use of the nasal pool-device). Furthermore, as the mucosa was thoroughly lavaged with saline after the tracer instillation procedure, uptake of tracer across the airway mucosa beyond the 15 min of exposure was prevented. The present measurements thus indicate solute absorption specifically across the nasal airway mucosa during a defined period of time. The nasal pool-device has been previously used for administration of known concentrations of agents onto a large and defined area of the nasal mucosal surface (Greiff et al., 1990). These methodological considerations are all necessary for the specific measurement of solute absorption across the airway mucosa.

Two previous studies have reported that house dust mite allergen increases airway epithelial permeability in vivo (Herbert et al., 1990, 1995). In a model where bovine bronchial epithelium was prepared and mounted in a two-chamber system increased flux of radio-iodine labelled albumin from the apical to the baso-lateral aspect was thus demonstrated in the presence of house dust mite allergen. In contrast, patients with perennial house dust mite allergic rhinitis, developing symptoms during the 4-week treatment withdrawal period (suggesting significant allergic disease), failed to present increased airway absorption in the present study. Several factors may explain why the findings in these two 'airway systems' differ although epithelial derangement may well occur in both. Exclusive to the in vivo condition epithelial injury is associated with instantaneous and high speed repair processes. Hence, epithelial restitution alone might prevent the development of a deranged absorption barrier (Persson et al., 1997). Perennial allergic rhinitis is also associated with microvascular-epithelial exudation that may neutralize the protease activity of house dust mite allergens already on the airway surface.

In conclusion, nasal airway absorption of the 1067 Da peptide desmopressin is not increased in perennial house dust mite allergic rhinitis compared with healthy subjects. This finding supports the notion that the airway mucosa in vivo maintains its barrier properties also in diseases with epithelial derangement and shedding.

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