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## Acute loss of lung function without wheezing during bee venom immunotherapy

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Short title: Bronchospasm during VIT

Bee venom immunotherapy (VIT) induces systemic reactions (1, 2). Bronchospasm is one of the possible adverse events. However, objective measures of bronchoconstriction have never been published during VIT. In particular, it is not known whether bronchoconstriction is associated with symptoms and/or decrease in lung function.

One patient (male, 15 yrs of age), the son of a beekeeper, without atopic symptoms but with occasional exercise-induced wheezing, presented three times with mild dyspnea during bee stings. However, severe dyspnea occurred after the sting. He was evaluated for possible allergy to bee venom. The patient had negative skin prick tests to the GA<sup>2</sup>LEN battery (3) but a positive intradermal skin test to bee venom (0.01 µg/ml, Stallergènes, Antony, France) and serum bee venom-specific IgE (>100 KUA/L, Phadia, Uppsala, Sweden).

VIT was initiated using Stallergènes extracts (Alyostal<sup>®</sup> *Apis mellifera*) with a cluster schedule (4). FEV<sub>1</sub> was monitored before and after VIT. During the second week of treatment, 15 min after a cumulative dose of 80 µg (30 + 50 µg), the patient developed an erythema, pruritus of the face and neck with dyspnea, cough and rhinitis, without any wheezing. There was no clinical sign of a severe asthma exacerbation (5), pneumothorax or extra-thoracic obstruction. Normal breathing sounds were heard. FEV<sub>1</sub> (with reliable expiratory manoeuvres) was immediately measured and a drop from 4.75 l to 3.7 l (18.5%) was found. However, there was only a marginal reduction of the FEV<sub>1</sub>/FVC from 100% to 91%. The patient received an oral H<sub>1</sub>-antihistamine, 60 mg prednisolone, 2 puffs of salbutamol, followed by an aerosol with terbutaline (5 mg) and ipratropium (0,5 mg), as well as oxygen via a mask (5 l/min). The dyspnea totally resolved after 20 min, and the erythema and rhinitis persisted for 1 hour. FEV<sub>1</sub> was measured 2 hrs after the onset of the reaction and had returned to baseline value (4.7 l).

A week later, the patient received 50 + 50 µg of venom and, within 20 min, developed a severe reaction with facial erythema, cough and dyspnea. There was strictly no wheezing and no clinical sign of a severe asthma exacerbation (5). FEV<sub>1</sub> dropped from 4.79 l to 3.0 l (37.3%) with a proportional reduction of FVC. The patient received an oral H<sub>1</sub>-antihistamine, 60 mg of prednisolone and two aerosols with terbutaline (2x5 mg) and ipratropium (2x0.5 mg) as well as oxygen via a mask (5 l/min). Adrenalin was not given. He completely recovered 30 min later. FEV<sub>1</sub> was measured 2 hrs after the onset of the reaction and had returned to baseline value (4.87 l).

To our knowledge, this is the first case that has been described of a patient suffering from a severe bronchoconstriction characterized by objective measurement without wheezing during VIT. Other causes of respiratory distress were very unlikely (extrathoracic obstruction, pneumothorax, acute pulmonary oedema...). Recovery without adrenalin is not usually observed in upper airway obstruction. Acute bronchoconstriction characterized by a drop in

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3 VC and a normal FEV<sub>1</sub>/FVC ratio has been observed in metacholine challenge in patients  
4 with asthma (6), as shown by the increase in residual volume representing airway closure.  
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6 We consider it important to report this case since it may occur more commonly than expected,  
7 and supports the regular use of FEV<sub>1</sub> or peak flow (PEFR) measurements in patients having  
8 suffered severe wheezing during a sting by hymenoptera. It is possible that non-atopic  
9 individuals react differently to asthmatics who may be more prone to wheezing.  
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