

Letter to the Editor

Tomato-induced occupational asthma in a greenhouse worker

To the Editor:

Tomatoes (*Lycopersicon esculentum*, botanical family of Solanaceae) are a well-documented source of IgE-mediated food allergy,¹ but only 1 report has suggested the possibility of an occupational respiratory allergy to tomato allergens.² Herein we report the clinical and immunologic findings in a tomato greenhouse worker who had occupational asthma and rhinitis.

A 33-year-old nonsmoking man had work-related rhinoconjunctivitis and asthma symptoms 4 years after starting employment in a greenhouse where tomatoes were grown in water-filled troughs for full-year cycles. He experienced chest tightness, wheezing, and cough while working in the greenhouse. He also reported severe rhinoconjunctivitis symptoms, including nasal and ocular itching, sneezing, rhinorrhea, and nasal blockage. These symptoms occurred about 3 hours after entering the greenhouse and improved after leaving the workplace, although asthma symptoms often recurred during the night. Over the following 2 years, the symptoms worsened progressively and no longer improved on weekends. The patient took an inhaled short-acting bronchodilator 3 to 4 times a day and an oral H₁-antihistamine almost daily. The subject did not identify the agent or process that caused his respiratory symptoms at work. He did not report any pre-existing or concurrent history of seasonal rhinitis. He could eat cooked and fresh tomatoes almost daily without experiencing any allergic reactions.

Skin prick testing was performed with self-prepared extracts of tomato plant components. The extracts of tomato flowers (including pollen), leaves, and stems were prepared by stirring the plant components (100 mg/mL) in saline for 1 hour at room temperature and passing them through a 0.15- μ m filtration membrane (Millipore Corp, Bedford, Mass). Skin prick tests with increasing dilutions (1:100, 1:10, and 1:1) of these extracts elicited a 7-mm immediate wheal response to the 1:1 flower extract and a 3-mm skin reaction to the leaf extract, although results were negative for stem extracts. Prick-to-prick testing with fresh tomato induced a 6-mm skin response. Skin prick testing with the tomato flower extract produced negative responses in 10 control subjects sensitized to grass pollen, birch pollen, or both.

Specific inhalation challenges were completed in the laboratory by using the tomato flower extract. Baseline spirometry showed an FEV₁ of 3.79 L (94% of predicted value) and an FEV₁/forced vital capacity ratio of 81%. A control challenge with inhaled saline did not induce any significant changes in FEV₁ over the following 6 hours (Fig 1). At that time, the histamine PC₂₀ value was measured at 3.9 mg/mL. The examination of induced sputum revealed a total cell count of 0.96×10^6 cells/mL, with eosinophils representing 0.5% of nonsquamous cells. On the following day, the subject was challenged by taking deep inhalations (2, 4, and 8) of stepwise concentrations of the tomato flower extract delivered through a dosimeter with an output of 5.9 μ L per inhalation (Spira Elektro-2; Respiratory Care Center, Hameenlinna, Finland). Eight breaths of the 1:10,000 dilution of the tomato flower extract resulted in a 31%

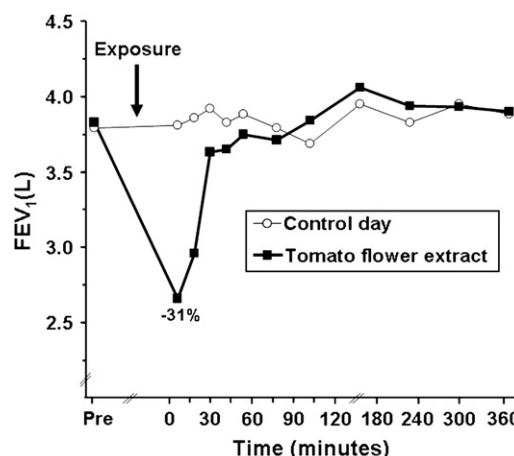


FIG 1. Results of specific inhalation challenges showing the changes in FEV₁ during a control day (open circles) and after inhalation of increasing concentrations of a tomato flower extract (8 breaths of the 1:10,000 dilution of the initial extract; solid circles).

decrease in FEV₁. Six hours after the end of exposure, the histamine PC₂₀ value was 1.85 mg/mL. A sputum sample collected 24 hours after challenge showed a significant increase in eosinophils (5.5% of 1.73×10^6 cells/mL). The subject left his job immediately after the diagnostic evaluation. Six months later, he was symptom free, his FEV₁ was 3.80 L (94% of predicted value), and his histamine PC₂₀ value was in the nonasthmatic range (>16 mg/mL).

The subject's serum exhibited specific IgE antibodies against tomato (7.3 IU/mL) and other plants belonging to the Solanaceae family, including potato (3.1 IU/mL), sweet bell pepper (2.1 IU/mL), eggplant (2.4 IU/mL), and chili pepper (1.9 IU/mL), as well as against natural rubber latex (2.7 IU/mL), mugwort (1.5 IU/mL), timothy grass (3.1 IU/mL), birch (2.8 IU/mL), and recombinant Bet v 1 (1.6 U/mL; ImmunoCAP method; Phadia Diagnostics, Uppsala, Sweden). Specific IgE antibodies against recombinant Phl p 7, Phl p 12, and Bet v 2 were not detected. Total serum IgE level was 564 U/mL.

Immunoblotting experiments with the tomato flower and pulp extracts were performed according to a previously described method,³⁻⁵ except that a horseradish peroxidase-labeled mouse anti-human IgE antibody was used for visualization. The patient's serum (Fig 2) showed a predominant IgE binding to proteins with molecular masses of 10, 22, and 28/30 kD in both extracts. Immunoblotting of the tomato pulp extract showed additional IgE binding to a 45-kD protein. Preincubation of the serum (1 hour at room temperature) with recombinant Bet v 1a (5 μ g/lane) and cross-reactive carbohydrate MUXF glycopeptide (10 μ g/lane) did not result in an inhibition of IgE binding (data not shown). The IgE-binding bands did not correspond to the currently characterized tomato allergens, including Lyc e 1 (a 14-kD profilin), Lyc e 2 (a 50-kD β -fructofuranosidase), and Lyc e 3 (a 9-kD nonspecific lipid transfer protein).³⁻⁵

As far as we know, this is the first report of a tomato-induced occupational airway allergy documented through a specific

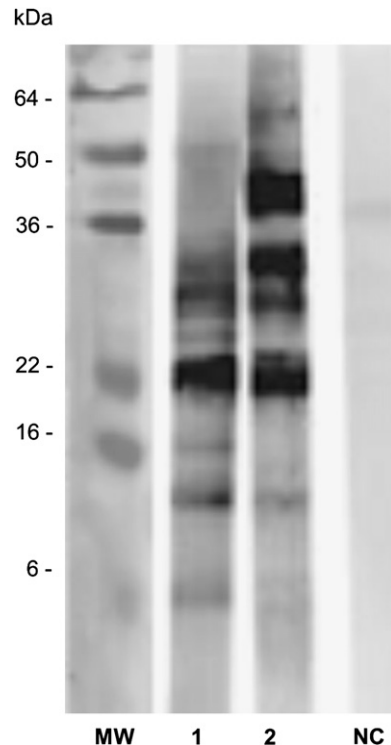


FIG 2. SDS-PAGE and IgE immunoblotting of the tomato flower (*lane 1*) and pulp (*lane 2*) extracts with the subject's serum. IgE-binding bands were detected at 10, 22, and 28/30 kD in both extracts. An additional IgE-binding band was also present at 45 kD in the pulp extract. *MW*, Molecular weight; *NC*, negative control serum.

inhalation challenge and immunologic studies. A 2-fold decrease in histamine PC₂₀ values and an increase in sputum eosinophil counts after inhalation challenge with the tomato flower extract supported a specific immunologic mechanism rather than a non-specific bronchial reaction. Greenhouse tomato growing has become a common practice in temperate areas because this process allows for a higher quality and a longer period of production. This report indicates that high-level exposure to tomato plant

materials should be considered a potential cause of IgE-mediated rhinitis and asthma. Further investigations are needed to estimate the prevalence and determinants of tomato-induced respiratory allergy among the exposed workforce, as well as to identify the clinically relevant allergens.

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REFERENCES

1. Larramendi CH, Ferrer A, Huertas AJ, Garcia-Abujeta JL, Andreu C, Tella R, et al. Sensitization to tomato peel and pulp extracts in the Mediterranean Coast of Spain: prevalence and co-sensitization with aeroallergens. *Clin Exp Allergy* 2008;38:169-77.
2. van Toorenbergen AW, Waanders J, Gerth Van Wijk R, Vermeulen AM. Immunoblot analysis of IgE-binding antigens in paprika and tomato pollen. *Int Arch Allergy Immunol* 2000;122:246-50.
3. Westphal S, Kempf W, Foetisch K, Retzek M, Vieths S, Scheurer S. Tomato profilin Lyc e 1: IgE cross-reactivity and allergenic potency. *Allergy* 2004;59:526-32.
4. Westphal S, Kolarich D, Foetisch K, Lauer I, Altmann F, Conti A, et al. Molecular characterization and allergenic activity of Lyc e 2 (beta-fructofuranosidase), a glycosylated allergen of tomato. *Eur J Biochem* 2003;270:1327-37.
5. Lorenz Y, Enrique E, Lequynh L, Fotisch K, Retzek M, Biemelt S, et al. Skin prick tests reveal stable and heritable reduction of allergenic potency of gene-silenced tomato fruits. *J Allergy Clin Immunol* 2006;118:711-8.

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