

sour- and bitter-flavored apple juice and broccoli, better than children who received a milk-based food during infancy.⁵

The next step will be to prospectively investigate the use of eHF and AAs on the development of food preferences in the long term and determine whether they are associated with picky eating behavior in food-allergic children. In conclusion, we found that the eHF-W tested had a better taste than the tested eHF-C and AA. Many factors contribute to the taste development of the child, and the influence of an eHF or an AA is not necessarily negative for taste development in these children.

Nicolette W. de Jong, PhD, BEd*

Aline B. Sprikkelman, PhD, MD†

Hanneke N.G. Oude Elberink, PhD, MD‡

Nicolette J.T. Arends, PhD, MD*

Berber J. Vlieg-Boerstra, PhD, RD†

*Department of Internal Medicine

Section of Allergology, Erasmus MC

Rotterdam, The Netherlands

†Department of Pediatric Respiratory Medicine and Allergy

Emma Children's Hospital

Academic Medical Center

University of Amsterdam

Amsterdam, The Netherlands

‡Department of Allergy
University Medical Center Groningen
University of Groningen
Groningen, The Netherlands
b.j.vlieg-boerstra@amc.uva.nl

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A case of anaphylaxis to palivizumab



Respiratory syncytial virus (RSV) is an enveloped RNA virus that is a common cause of upper respiratory infections in early childhood.¹ Patients with congenital heart disease, preterm birth, and chronic lung disease of prematurity are at increased risk for severe disease with RSV infection, which results in an estimated 57,527 hospitalizations annually in children younger than 5 years.² Palivizumab is the only licensed product available for the prevention of RSV in those pediatric patients at increased risk of severe disease from RSV. Palivizumab is a humanized monoclonal antibody (mAb) consisting of a human IgG1 framework combined with murine complementarity determining regions for the A antigenic site of the F fusion protein of the RSV. It is administered intramuscularly once every 30 days, for a total of 5 doses.³ Palivizumab has an excellent safety profile, and in 2 large phase III trials there were no reports of anaphylaxis. Post-marketing analysis has continued to confirm the safety profile of palivizumab, with no cases of anaphylaxis identified in the literature. We report the first case of anaphylaxis followed by urticaria associated with the administration of palivizumab.

The patient was a 2-year-old girl with DiGeorge syndrome, tetralogy of Fallot, and chronic lung disease of prematurity who depended on a ventilator. Given her congenital heart disease and chronic lung disease of prematurity, she was started on monthly palivizumab during her first year of life. She received a total of 5 doses that year without any complications. However, the next year, at 2 years of age, 20 minutes after her second dose, she developed nonbilious emesis that was accompanied by dyspnea and cough. Over the course of the next few minutes, the patient developed diffuse urticaria and angioedema of her eyelids, prompting activation of the clinic's rapid response system. The response team found the patient to be hypoxic, hypotensive, and tachycardic. She immediately

received supplemental oxygen and 0.15 mg of epinephrine intramuscularly. Over the course of a few minutes, her symptoms markedly decreased. She was transported to the pediatric intensive care unit for overnight observation. Before the day of the reaction, the patient had been well, with no preceding illness, recent fevers, new medications, and significant changes in her health.

By the time of bedside consultation by an allergist approximately 4 hours after the first onset of symptoms, the patient still exhibited a few scattered hives near the injection site of the palivizumab but was otherwise well, with stable vital signs and no increased oxygen requirement. Although a tryptase level was obtained, it was not drawn until several hours after the resolution of symptoms and was found to be within normal limits. She was monitored overnight and treated with a 2-day course of antihistamines and oral steroids. Strict avoidance of palivizumab was recommended. Approximately 1 week later, she had a 2-week period when she had frequent episodes of isolated urticaria without any systemic symptoms. At approximately this time, she was diagnosed with a mild upper respiratory tract infection without radiographic changes. After 2 weeks, the urticaria resolved and she has not experienced any further episodes of anaphylaxis or urticaria.

Although chimeric mAbs such as palivizumab carry immunogenic potential, because they are foreign proteins of sufficient size, true IgE-mediated hypersensitivity reactions are uncommon.⁴ Palivizumab has a strong record of safety with no prior reports of anaphylaxis identified in the literature. Given the present patient's quick onset of symptoms after the administration of palivizumab, cutaneous involvement, respiratory compromise, hypotension, and rapid improvement after the administration of epinephrine, her symptoms fulfill the criteria for the definition of anaphylaxis.⁵ Because her reaction was so severe, further investigation was deemed unlikely to change the recommendation for strict avoidance of palivizumab; however, future evaluation for human anti-mouse or antihuman antibodies may provide insight into potential risks regarding any future mAb therapies should the need arise. The continued episodes of urticaria after the episode of anaphylaxis

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could have several etiologies. Protracted anaphylaxis and delayed infusion reactions to mAbs are well described in the literature; hence, the urticaria may have represented a continuation of her anaphylaxis.^{6,7} Other possibilities include priming of her immune system from her episode of anaphylaxis or the recurrent episodes of urticaria may have been completely unrelated to her episode of anaphylaxis. As the use of mAbs such as palivizumab continues to increase, so, too, will the reported incidence of adverse reactions, and it is important for providers to recognize the potential for IgE-mediated hypersensitivity reactions with the use of mAbs.

Julia Savitz, MD
Casey Geaney, MD
Taylor A. Banks, MD

Department of Allergy/Immunology and Immunizations
Walter Reed National Military Medical Center
Bethesda, Maryland
julia.savitz@med.navy.mil

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Systemic reactions to honeybee stings and nonsteroidal antiinflammatory drugs



Hymenoptera stings are an important cause of morbidity, which is clinically expressed by large local reactions and systemic reactions (SRs), the latter including life-threatening anaphylaxis.¹ The major pathophysiologic mechanism that underlies the reaction is IgE-mediated sensitization, but a number of factors were reported to favor SRs to stings. Among these factors, high baseline serum tryptase concentrations (which are usually associated with mast cell disorders) and the risk of more severe reactions in elderly people are generally agreed to play a role,^{1,2} whereas other parameters, such as male sex and atopy, are debated. Moreover, there are single reports concerning associations between SRs to stings and factors such as physical exercise,³ blood eosinophilia in children,⁴ and consumption of antihistamines by beekeepers before attending the hives.⁵ As far as the role of drugs in favoring SRs to stings is concerned, angiotensin-converting enzyme (ACE) inhibitors were associated with SRs, leading to the recommendation to replace them with other medications in venom-allergic patients.^{1,2} However, other studies did not confirm the responsibility of ACE inhibitors and β -blockers as well, at least in severe SRs.⁶

We report 3 cases of SRs to bee stings exclusively occurring after taking nonsteroidal antiinflammatory drugs (NSAIDs). The first case concerns a 58-year-old female beekeeper who for many years received regular bee stings with no reaction. She was stung by a bee 3 hours after taking 80 mg of ketoprofen and experienced urticaria-angioedema, with no mucosal involvement. The reaction was treated by antihistamines and receded in approximately 5 hours. She had taken the drug previously and resumed it subsequently with no reaction. Further bee stings with no consumption of NSAIDs were completely tolerated. Intradermal skin test results were positive to bee venom at 0.1 μ g/mL.

The second case was a 34-year-old male beekeeper, who never had reactions of any type to stings until the day he took 80 mg of ketoprofen. He experienced urticaria-angioedema 3 hours after a sting, with no mucosal involvement and spontaneous resolution in 2 hours. As in the first case, no reaction occurred to taking ketoprofen or bee stings alone before and after the reaction. Intradermal skin test results were positive to bee venom at 0.01 μ g/mL.

The third case was a 78-year-old male beekeeper with a history of numerous bee stings for many years with no reaction. Five hours after taking 1 g of aspirin, he was stung by a bee and developed urticaria-angioedema with no mucosal involvement. The reaction was treated by antihistamines and receded in approximately 6 hours. As in the other cases, he subsequently did not have any reaction to stings or aspirin. Intradermal skin test results were positive to bee venom at 0.01 μ g/mL.

Considering that NSAIDs are among the most frequently used drugs worldwide and specifically are the best-selling over-the-counter drugs, it seems difficult to explain how NSAIDs have never been found to be a risk factor for allergic reactions to stings. However, NSAIDs are often taken for common symptoms, such as headache; thus, it is likely that consumption goes unreported when the physician collects the clinical history from patients, including those with reactions to insect stings. The 3 cases we present are similar. All patients were beekeepers with a history of countless bee stings with no reaction. They had positive intradermal test results to bee venom, and they had used NSAIDs with no adverse effect. One may argue that these cases simply confirm the natural history of Hymenoptera venom allergy by which a systemic reaction, particularly urticaria-angioedema, is spontaneously followed by tolerance to further stings.⁷ However, natural history of allergy in beekeepers seems different because the reactivity to stings, which is relatively common in the early phase of beekeeping, turns to tolerance with further stings and especially when the number of stings is more than 50 per year.⁸ Thus, it is unlikely that the 3 beekeepers we describe, each of whom had received hundreds of stings, started off with allergy without other favoring factors. Actually, it was this unlikelihood, along with the tolerance to subsequent bee stings, that led us to search for possible risk factors. Indeed, NSAIDs were recently reported as a cofactor in allergic reactions to plant foods, their use being reported by 33% of patients with such reactions.⁹ The patients we studied had no history of food allergy. In addition, they reported having eaten their usual foods the day of the reaction and that they ate these foods again subsequently with no symptom(s). The change in mucosal permeability induced by NSAIDs, possibly increasing the food allergen absorption, was suggested as a conceivable mechanism in NSAID-enhanced food allergy.¹⁰ However, this cannot account for the reactions to bee stings we observed, the pathophysiology of which needs to be investigated.