Anaphylactic Shock to a DEET-Containing Insect Repellent

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In recent decades, increased awareness of many insect-borne diseases (eg, malaria, dengue hemorrhagic fever, and West Nile virus) has generated a rapidly growing number of insect repellents in order to prevent transmission. N-N-diethyl-3-methylbenzamide, otherwise known as N,N-diethyl-meta-toluamide, diethyltoluamide (DEET), is a reliable option [1]. DEET was originally patented in 1946 by the US Army for military use in insect-infested areas and subsequently registered in 1957 for use by the general public. The properties of DEET have led it to be considered the best protection against arthropod-borne diseases, and it is now the major active ingredient in most topical insect repellents [2].

Despite the widespread use of DEET as an insect repellent, it has caused very few cases of contact urticaria [3-7] or urticaria [8], and, to our knowledge, only 1 case of anaphylaxis caused by DEET was published in 1982 [9]. We report a case of anaphylactic shock after application of an insect repellent containing DEET in which the allergology study yielded positive results.

A 28-year-old woman with a previous history of allergic rhinoconjunctivitis and asthma and sensitization to pollens experienced tingling of the lips after indirect airborne contact with an insect repellent known commercially as Medcell (water, diethyltoluamide, ethylthexyl methoxycinnamate, ethylhexyl salicylate, methylene bis-benzotriazolyl, tetramethylbutylphenol, mineral oil, isopropyl myristate, cetyl alcohol, glyceryl stearate/PEG-100 stearate, cetyl acetate/acetylated lanolin alcohol, isopropyl palmitate, methylparaben, fragrance of benzyl benzoate and coumarin, triethanolamine, propylparaben, carbomer). A few minutes later, the patient applied the same insect repellent on her legs. She immediately developed labial edema, dyspnea, dysphagia, generalized rash, and dizziness. Assessment in the emergency department revealed tachycardia, tachypnea,

and blood pressure of 90/40 mm Hg. She was treated with intravenous hydrocortisone (200 mg), dexchlorpheniramine (5 mg), ranitidine (50 mg), intramuscular epinephrine (0.7 mg), fluid therapy, and nebulized budesonide and salbutamol. In the absence of improvement, the patient was admitted to the critical care unit, although her condition improved within a few days. Serum tryptase was not measured during the reaction.

She was subsequently referred to our department, where an allergology study was performed 1 month after the reaction. We took a detailed history, which allowed us to rule out the simultaneous use of other drugs and the presence of possible cofactors. The allergology study was based on a high suspicion of causality for the repellent solution applied to the skin. The basal serum tryptase level was normal (2.76 µg/L).

An open patch test was performed by applying a small drop of the repellent solution on the patient's forearm. The same test yielded negative results in 5 atopic controls. A basophil activation test (BAT) based on whole blood was performed with the repellent solution and with DEET. Both substances were tested along a dose-response curve using several dilutions. Double staining was performed with CD203c-PE to select the basophil population and CD63-FITC to measure basophil activation.

Thus, the investigation was extended using a dot blot assay. After dilution in phosphate-buffered saline (PBS), the extracts were coated on a nitrocellulose membrane using a 96-well dot-blot system. The membrane was removed from the device and blocked in PBS-Tween 20 0.5% for 1 hour at room temperature. The membrane was then incubated overnight with patient serum (dilution 1/5 in PBS-Tween 20, 0.5% at 4ºC). Finally, a dot blot inhibition assay was performed after preincubating the patient's serum (diluted 1/5) for 30 minutes with different concentrations of DEET extract.

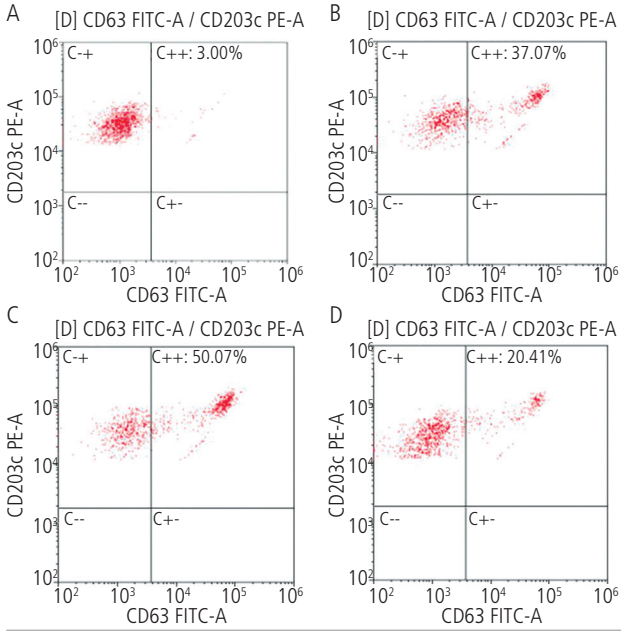

Figure. Basophil activation test with DEET and Medcell. The C++ quadrant of the dot plots represents the percentage of basophils that express CD63 at high intensity (activation of cells). A, Negative control. B, positive control. C, Medcell at dilution 1/80. D, DEET at dilution 1/80.

Open patch testing with a small drop of Medcell repellent led to erythema and a wheal of 6 × 3 cm within a few minutes. The CD63 BAT, which was conducted with Medcell and with DEET, yielded a positive response for both DEET and Medcell (Figure and Figure E1 in the Online Repository).

Dot blot assay was also positive for DEET and for Medcell. The recognition of the repellent solution in its entirety was greater than that of isolated DEET (Figure E2 in the Online Repository). Finally, the dot blot inhibition assay revealed total inhibition of specific IgE to the repellent with DEET (Figure E3 in the Online Repository).

Based on the clinical history and allergology study results, the patient was diagnosed with an anaphylactic reaction to DEET. We subsequently advised her to check the excipients of repellent solutions to ensure that they did not contain DEET.

Hypersensitivity reactions associated with DEET insect repellent are very unusual, with almost all cases involving contact urticaria [3-7] or urticaria [8]. To date, the only case of anaphylaxis caused by DEET was that reported by Miller [9] in 1982. A 42-year-old woman touched a companion who had just sprayed himself with an insect repellent containing DEET. She experienced generalized pruritus, generalized angioedema, and nausea and eventually lost consciousness. In the emergency room, her blood pressure was 70/40 mm Hg.

The main diagnostic tool comprises a detailed history and skin test (open patch test on the forearm) showing a causal relationship with DEET. Very few in vitro studies with DEET have been performed. Galassi et al [6] presented the first positive BAT result with DEET in a case of contact urticaria in a 50-year-old woman who had an urticarial reaction to multiple DEET-based insect repellents. She reported an urticarial rash on the exposed areas a few minutes after application of the spray, aerosol, or lotion containing DEET. Wantke et al [8] searched unsuccessfully for the presence of specific IgE to DEET using ELISA in the case of a 4-year-old boy who, shortly after applying DEET (contained in an insect repellent called Anti-Muckenmilch) to his legs and forearms, developed generalized itch and urticaria and also wheezed and coughed for 30 minutes.

In conclusion, we report a case of very severe anaphylactic reaction to DEET contained in an insect repellent solution. The condition was diagnosed based on the clinical history and a positive open patch test result, positive BAT results to DEET, and a dot blot assay. Dot blot inhibition assay also revealed total inhibition of specific IgE to the repellent with DEET. These data suggest an IgE-mediated immunological mechanism. To our knowledge, this is the first case of anaphylaxis to DEET with a positive result in an in vitro study.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

Previous Presentation

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