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Generalized urticaria induced by a diethyltoluamide-containing insect repellent in a child

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Diethyltoluamide (DEET) is used worldwide in insect repellents. Pure DEET is irritant to skin and mucous membranes. However, the concentrations used in consumer products rarely induce contact dermatitis or urticaria (1-4).

Case Report

A 4-year-old boy was stung by mosquitoes. Shortly afterwards, the insect repellent Anti-Mückenmilch was applied to his legs and forearms. Minutes later, generalized itch and urticaria developed and the boy wheezed and coughed for about 30 min. He was taken to a general practitioner who applied a topical antihistamine. The wheals had gone by the following morning.

Anti-Mückenmilch, Gel tropic version[®] (Jaico, Belgium), was applied as an open patch test. In addition, the boy was prick-tested against Anti-Mückenmilch, mosquito (*Culex pipiens*), histamine 10 HEP and saline solution (negative control). Reading was done after 20 min. Total IgE, specific IgE against mosquito (*Culex*

pipiens) by RAST, and specific IgE against DEET by ELISA were assessed.

A closed patch test against the insect repellent Anti-Mückenmilch, containing 25% DEET, was also performed on the boy's forearm, using Cura Test[®]. In addition, consecutive concentrations of DEET (Sigma Chemicals, St. Louis, USA) in ethanol 35% and another repellent (Autan Lotion[®], Bayer, Germany), containing 20% DEET, were so tested. Substances remained on the skin for 20 min, were then removed, and readings were made after 0, 10, 20 and 50 min.

To exclude irritant effects of the DEET test preparations, a closed patch test was also performed in 10 adult controls.

On open testing, Anti-Mückenmilch did not react. On prick testing, Anti-Mückenmilch and mosquito extract did not react, but a 10-mm diameter wheal to histamine, with 3 satellite wheals, as well as a 2 mm wheal to saline, with a widely spreading erythema, developed. Total IgE was elevated to 70 kU/l (≤ 20 kU/l). Lung function was in the normal range. No specific IgE against DEET or mosquito was found.

Closed patch testing revealed a flat erythematous reaction to Anti-Mückenmilch but no wheal. Concentration-independent flat erythematous reactions were seen to all concentrations of DEET, but also to Autan Lotion[®] as well as to ethanol 35%, persisting for at least 50 min (Table 1). 7/10 controls showed slight erythematous reactions to DEET 25.0% and 20.0% for 5 min.

Discussion

The maximum concentration of DEET in insect repellents is limited to 25%, as higher concentrations may induce irritant skin reactions. In Austria, according to an agreement between all manufacturers, DEET-containing repellents should not be used in children below 6 years of age (5).

In our patient, insect repellents had never been used before. As he showed generalized urticaria and wheezing

Table 1. Skin reaction after 20 min of closed patch testing; no wheals developed

	0 min	10 min	20 min	50 min
Erythema				
Jaico Anti-Mückenmilch [®]	+++	+++	++	+
Autan Lotion [®]	+++	+++	++	+
diethyltoluamide				
25.0%, 12.5%, 6.25%, 3.12%	+++	+++	++	+
20.0%, 10.0%, 5.0%, 2.5%	+++	+++	++	+
ethanol 35.0%	+++	+++	++	+
Cura Test	-	-	-	-
Controls				
diethyltoluamide 25.0%	+ 7/10	-	-	-
diethyltoluamide 20.0%	+ 7/10	-	-	-
ethanol 35.0%	-	-	-	-
Cura Test	-	-	-	-

minutes after the application of the repellent, allergic contact urticaria, as previously described (1, 2), appeared to be the most likely diagnosis. However, negative test results excluded type-I allergy. Urticaria after mosquito bites had never occurred in the boy and type I allergy against mosquito could not be detected.

Results of the closed patch test revealed persistent non-specific erythematous reactions against Anti-Mückenmilch and all other substances, including ethanol (6), indicating high sensitivity of the boy's skin. Erythema occurring in 7/10 controls against diethyltoluamide 25.0% and 20.0% was weak and transient. As we also found distinct wheal and flare reactions to histamine and saline on skin prick testing, the patient clearly shows non-specific cutaneous hyperreactivity, which may have been the cause of his urticarial reaction.

Because we could not elicit type-I allergy to Anti-Mückenmilch or diethyltoluamide, we conclude that the boy seemed to have developed non-immunologic, chemi-

call-induced generalized urticaria from the insect repellent.

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Type-IV hypersensitivity to topical estradiol in a patient tolerant to it orally

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Transdermal therapeutic systems (TTS) (1) have become available for more and more drugs, including scopolamine, nitroglycerine, nicotine, clonidine, and estradiol (2). With estradiol, about 1/5 of patients report side-effects (3), though allergic reactions are rare and usually not caused by the active drug.

Case Report

A 55-year-old Caucasian woman had been on an oral estrogen, Presomen compositum[®] (active ingredients: 55% estron, 28% equilin, 5% estradiol, 9% dihydroequilin, 3% equilenin and dihydroequilenin). Although no side-effects occurred, this was changed to the TTS Estraderm TTS25[®] (active ingredient: 17- β -estradiol) applied 2 $\times$ weekly. During application of the 9th system, an itchy erythema appeared at the site of application, followed by generalization of the erythema, which became more urticarial. Because of this side-effect, she was switched back to Presomen compositum[®] which again she tolerated well.

Estraderm TTS25[®] shares the basic structure of all TTS: consisting of an outer impermeable membrane, a reservoir containing the solubilized drug (in this case, 17- β -estradiol in ethanol, together with the gel-forming poly-o-hydroxypropylcellulose), a rate-limiting membrane, and an adhesive.

Following resolution of cutaneous symptoms, a patch

test with the complete Estraderm TTS25[®] system was initially performed, yielding a positive result after 3 days. Patch tests with separate components of the system were then carried out (Table 1). Negative results were recorded to poly-o-hydroxypropylcellulose at 1% and 2% in ethanol, as well as the adhesive polyisobutylene at the same %s in benzene. Furthermore, the respective vehicles, ethanol and benzene, failed to elicit positive reactions. In contrast, the active ingredient 17- β -estradiol yielded positive patch test results at various concentrations (1%, 2%, and 4%, in 96% ethanol). The same concentrations did not elicit positive reactions in 10 volunteers patch tested for other reasons.

Table 1. Results of patch tests at D3

Estraderm TTS25 [®]		++
poly-o-hydroxy-propylcellulose	1% in ethanol 30%	-
	2% in ethanol 30%	-
polyisobutylene (adhesive)	1% in benzene	-
	2% in benzene	-
test vehicles	benzene 100%	-
	ethanol 96%	-
17- β -estradiol	1% in ethanol 96%	+
	2% in ethanol 96%	+
	4% in ethanol 96%	+++*

* Negative in 10 controls.

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