

Table 1. The rate of positive reaction to oxidized *d*-limonene on patch testing

Ref.	Study population	Patch test materials	n	Positive rate
Meding et al. (5)	car mechanics with hand eczema	oxidized <i>d</i> -limonene 5% pet.	105	2/105 (1.9%)
Karlberg & Doooms-Goossens (6)	patch test patients	oxidized <i>d</i> -limonene 2%, 3%, or 5% pet.	2800	49/2800 (1.8%)
		<i>d</i> -limonene hydroperoxides 0.5% or 1% pet.	1554	23/1554 (1.5%)
Chang et al.	patch test patients	oxidized <i>d</i> -limonene 2% pet.	88	2/88 (2.3%)

Finland). The patches were applied to the back for 2 days and read at 4 days. He had ++ reactions to oxidized *d*-limonene 2% and 1% pet.. Upon discontinuing the use of his *d*-limonene hand cleanser, his hand eczema resolved.

Discussion

Karlberg et al. (1) have done extensive research on *d*-limonene. In guinea pigs, *d*-limonene of high purity gave no significant allergic reaction, while *d*-limonene exposed to air for 2 months sensitized animals. Gas chromatographic analyses indicated that the content of limonene oxide in *d*-limonene increased with prolonged air exposure (1). Some oxidation products of *d*-limonene, R-(-)-carvone and a mixture of cis and trans isomers of (+)-limonene oxide, and hydroperoxides in oxidized *d*-limonene, were identified as potent contact allergens (2, 3). The addition of the antioxidant butylated hydroxytoluene (BHT) prevented autooxidation of *d*-limonene for periods depending on the purity of *d*-limonene and room temperature (4). Cold storage in closed vessels was recommended to avoid prolonged air exposure and oxidation of *d*-limonene which enhance sensitization.

105 car mechanics with hand eczema were patch tested to a standard series and a special car mechanics series: 2 reacted to oxidized *d*-limonene (5). A study performed in Stockholm and Belgium showed that, among dermatitis patients, 1.1% to 2.4% reacted to oxidized *d*-limonene, and 0.9% to 2.8% reacted to *d*-limonene hy-

droperoxide on patch testing (6). In our screening, 2 of 88 patients (2.3 %) reacted to oxidized *d*-limonene; probable relevance was documented in 1 (this case report). The rates reported of positive reaction to oxidized *d*-limonene on patch testing are shown in Table 1. With the increasing use of *d*-limonene, dermatologists might consider adding oxidized *d*-limonene to a hand eczema series.

References

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The provocative use test (PUT) [repeated open application test (ROAT)] in topical corticosteroid allergic contact dermatitis

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Allergic contact dermatitis from corticosteroids has been found in 2% to 6% of patients attending contact dermatitis clinics (1-5). Cross-reactions occur more frequently within the same structural group (6-7), which is supported by conformational analysis (8).

Case Report

A 46-year-old woman had eczema of lower limbs, hands, and hips recalcitrant to treatment intermittently for years. Flare-up of dermatitis was noted after taking oral

Table 1. Initial patch test results

	Conc. %	D2	D4	D5
Westcort cream as is (hydrocortisone valerate 0.2%)		—	+	++
budesonide 0.1% pet.		—	++	++
Pivalone spray		—	—	++
budesonide	0.1	—	++	NT
betamethasone-17-valerate	1.0	—	++	NT
triamcinolone acetoneide	1.0	—	++	NT
tixocortol-21-pivalate	1.0	+	—	NT
alclomethasone-17,21-dipropionate	1.0	—	—	NT
clobetasol-17-propionate	1.0	—	++	NT
dexamethasone-21-phosphate disodium salt	1.0	—	+	NT
hydrocortisone-17-butyrate	1.0	—	++	NT

*NT: not tested.

prednisone. Patch tests were performed with an extended standard series and her skin care products, utilizing 8-mm Finn Chambers on Scanpor (Epitest Ltd., Finland) left on the back for 2 days. Readings were at 2, 4, and 5 days, and reactions were scored in accordance with

ICDRG guidelines. The positive reactions are shown in Table 1. She was negative to tixocortol-21-pivalate 1% pet., and the excipients included in the extended series.

Subsequently, patch tests with a commercial corticosteroid series (Chemotechnique-Dormer Laboratories

Table 2. Patch test and PUT of commercial corticosteroids formulations

		D2	D4	ROAT
alclometasone dipropionate:	Aclovate oint 0.05%	—	++	positive
	Aclovate cream 0.05%	—	+	NT
amcinonide:	Cyclocort cream 0.1%	—	++	positive
betamethasone benzoate:	Diprolene gel 0.05%	—	+++	NT
	Diprolene cream 0.05%	—	+	NT
	Diprolene oint 0.05%	—	++	positive
clobetasol propionate:	Temovate cream 0.05%	—	+	NT
	Temovate oint 0.05%	—	++	NT
	Cormax oint 0.05%	NT	NT	positive
clocortolone pivalate:	Cloderm cream 0.1%	—	—	positive
desonide:	DesOwen oint 0.05%	—	++	NT
desoximethasone:	0.25% oint	NT	NT	positive
	Topicort cream 0.25%	—	+	NT
	Topicort gel 0.05%	—	++	NT
diflorasone diacetate:	Florone cream 0.05%	—	++	NT
	Florone E cream 0.05%	—	++	NT
	Psorcon oint 0.05%	—	++	NT
fluocinolone acetoneide:	Synalar solution 0.01%	—	+/-	NT
	Synalar oint 0.025%	—	+	NT
	Synemol cream 0.025%	—	++	NT
fluocinonide:	Lidex cream 0.05%	—	+++	NT
	Lidex E-cream 0.05%	—	+	NT
	Lidex gel 0.05%	—	++	NT
	Lidex solution 0.05%	—	++	NT
	Lidex oint 0.05%	—	++	positive
	Fluonex cream 0.05%	—	++	NT
fluticasone propionate:	Cutivate cream 0.05%	—	++	NT
	Cutivate oint 0.005%	—	++	positive
halobetasol propionate:	Ultravate cream 0.05%	—	++	NT
	Ultravate oint 0.05%	—	++	NT
mometasone furoate:	Elcon lotion 0.1%	—	++	NT
	Elcon oint 0.1%	—	++	positive
hydrocortisone:	Lacticare-HC lotion 1%	—	—	NT
	Lacticare-HC lotion 2.5%	—	—	NT
hydrocortisone acetate:	1% oint	NT	NT	negative
HC-acetate 2.5%+pramoxine 1%:	Pramosone lotion	NT	NT	negative
hydrocortisone butyrate:	Locoid oint 0.1%	NT	NT	positive
betamethasone valerate:	0.1% oint	NT	NT	positive
flurandrenolide:	Cordran tape	NT	NT	positive
halcinonide:	Halog oint 0.1%	NT	NT	positive
hydrocortisone buteprate:	Pandel cream 0.1%	NT	NT	positive
prednicarbate:	Dermatop emollient cream 0.1%	NT	NT	negative
triamcinolone acetoneide	0.1% oint	NT	NT	positive

Inc., Sweden) and a UCSF corticosteroid series were performed (Tables 1, 2). The UCSF corticosteroid series is composed of 32 commercial topical corticosteroids. To rule out false-positive and false-negative reactions, and to define the appropriate topical corticosteroid to the patient, the corticosteroids that were positive or negative on patch tests were subjected to provocative use tests (PUT). Other commercially-available topical corticosteroids, with chemical structures different from those in our corticosteroid series were also chosen for provocative use tests, consisting of 2× daily application to the volar forearm for up to 2 weeks (Table 2).

Discussion

This patient was allergic to 23 corticosteroids (patch and/or use tests) but seemed to tolerate hydrocortisone, tixocortol-21-pivalate, and prednicarbate, as evidenced by negative patch and/or use tests. Tixocortol-21-pivalate is considered a marker of hydrocortisone allergy (8–9). The + reaction to tixocortol pivalate at D2 at the second patch test could have been irritant. The ++ reaction to Pivalone spray (containing tixocortol-21-pivalate) at D5 at the 1st patch test could have been false-positive due to another ingredient. The negative reaction to alclomethasone-17,21-dipropionate could have been false-negative. Clcortolone pivalate 0.1% was negative on patch testing but was positive on PUT. The test concentration, vehicle choice, absorption of corticosteroid through skin, anti-inflammatory effect of corticosteroids, impurities, and time of reading could contribute to false-negative or false-positive reactions on patch testing.

Whether allergy to the product exists or not is an important issue for the patient. Most modern commercial corticosteroids have optimized vehicles to increase penetration. Since there are still controversies about patch testing with corticosteroids, PUT with the commercial products is a practical approach for a patient with suspected allergic contact dermatitis from corticosteroids. Considering the multiple allergies and cross-reactions of corticosteroids and incomplete standardization in patch test methodology, and in attempt to define safe products for the patient, we performed extended PUT on this patient.

Wilkinson et al. (10–12) suggested intradermal tests to confirm positive patch test reactions, to detect sensitivity to other corticosteroids and to detect false-negative reactions on patch testing.

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