

allergic reactions to DMPA, CAPB seeming to play the greatest rôle, while APG does not show any such carrier effect; (ii) the more concentrated the surfactants and DMPA, the greater the effect on the number of reactions, the type of surfactant, however, seeming to be the key factor.

From the results of group 4, it can be concluded that: (i) blends of CAPB with other surfactants reduce the carrier effect of the higher concentration of betaine; (ii) also in the case of blends, the more concentrated the surfactants and DMPA, the greater the effect, which could be related to the increased irritant effects of more concentrated solutions of surfactants; (iii) APG is very efficient in reduction of reaction elicitation.

Comparing the results of groups 3 and 4, it can be seen that, to reduce allergic reaction risk, betaine should be blended with APG (or with other non-ionics, to be tested in the future). Careful monitoring of DMPA content in commercial betaines should also be routinely performed.

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Active sensitization to budesonide and para-phenylenediamine from patch testing

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Case Report

A 39-year-old man, with a single episode of hand and foot eczema 1 year ago, was referred with a subacute hand eczema. He had often received oral paracetamol and piroxicam for ankylosing spondylitis. As he worked at an aircraft motor plant, he currently used latex gloves to avoid contact with motor oils. The patient was tested with the European standard series (Trolab[®], Hermal, Reinbek, Germany), his ointment, motor oil 10% in olive oil (closed test) and as is (semi-open test). We added budesonide 0.1% pet. (Trolab[®]), tixocortol pivalate 1% pet. (Laboratoires Jouveinal, Fresnes, France) and hydrocortisone-17-butyrate 1% eth. (Laboratoires Yamanouchi, Charenton-le-Pont, France) to detect corticosteroid (CS) sensitivity, and an ethanolic CS mixture containing budesonide 0.05%. Patch tests removed at D2 showed a non-relevant + reaction at D3 to balsam of Peru, a ?+ reaction to fragrance mix, and weak transient telangiectasia at the budesonide and Diprosone[®] cream sites (this latter containing betamethasone 0.05%). The lesions rapidly cleared and we diagnosed an irritant contact dermatitis from motor oil.

The patient was examined at D17 since he had noted 2 pruritic lesions on his back for 2 days. We observed 2 flare-up reactions. The 1st was erythematous and oedematous and the 2nd, thought to corre-

spond to budesonide, showed some crusts and scaling. A repeat patch test session was performed 6 days later (without the motor oil, and with hydrocortisone-17-butyrate being diluted 0.1% in pet.), with additional serial dilutions of budesonide (Laboratoires Astra, Nanterre, France) 0.1 down to 0.0001% eth., each set in square chambers (Van der Bend). Results reported in Table 1 indicated that the late positive reactions were due to both budesonide and para-phenylenediamine (PPD). The CS mixture was tested with a + reaction at D2. A 3rd patch test session was performed 2 months later, with CS belonging to the B group (amcinonide, budesonide, desonide, flunisolide, halcinonide and triamcinolone acetonide) according to their chemical structure (1–3). Serial dilutions of 1, 0.1, 0.01, 0.001, and 0.0001% were made at the same time with the different CS in ethanol 95°. We also tested a blank with ethanol and CS from the D group (clobetasol, betamethasone 17-valerate and betamethasone dipropionate, each 0.1% ethanol) in square chambers. Reactions quoted as recommended by the ICDRG at D2, D4, and D8, indicated sensitivity to budesonide only (Table 1). A ROAT was finally performed with a commercial cream containing 0.05% desonide, and with a 0.05% fluocinonide ointment, both applied 2× per day, on the left and on the right forearm, respectively. There were no reactions after 7 days.

Table 1. Results of patch testing in the patient

	1st session D2/D3	2nd session D2 (D23/D3 (D24)	3rd session D2/D4/D8
para-phenylenediamine 1% pet.	—	+/+	NT
balsam of Peru 25% pet.	—/+	+/+	NT
fragrance mix 8% pet.	—/?+	?+/+	NT
budesonide 0.1% pet.	—	?+/+	NT
budesonide 1% eth.	NT	+/+	NT
budesonide 0.1% eth.	NT	+/+	NT
budesonide 0.01% eth.	NT	?+/+	+/+/+
budesonide 0.001% eth.	NT	?+/+	+/+/+
budesonide 0.0001% eth.	NT	—	?+/?+/-
budesonide 0.00001% eth.	NT	NT	—
budesonide 0.000001% eth.	NT	NT	—
hydrocortisone-17-butyrate	—	—	NT
amcinonide, desonide, flunisolide, halcinonide, triamcinolone acetonide (1% down to 0.0001% eth.)	NT	NT	—
clobetasol, betamethasone-17-valerate, betamethasone dipropionate (0.1% eth.)	NT	NT	—

Discussion

Active sensitization (AS) is a known complication of patch testing, generally asymptomatic, or suspected when a flare-up occurs. The positive, often non-pruritic, reaction is observed more than 7 days after application, but recurs within 3 days after reapplication. AS has been described with substances such as PPD, isothiazolinones, sesquiterpene lactones and (meth)acrylates (4–6), and recent cases were suspected as being due to gold sodium thiosulfate (7). AS rarely occurs with substances in the standard series and when proper techniques are used, and results mainly from additional testing at excessive concentrations (4–6).

Budesonide is a blend of 2 diastereoisomers commonly used to detect sensitivity to corticosteroids (CS) from both the B and D groups (1, 8, 9). This is, to our knowledge, the 1st case of AS to budesonide from patch testing to be reported. Sensitization to PPD, though simultaneous, is less surprising. However, a French author has observed late positive reactions to budesonide in 2 patients, during a systematic late patch test reading (Martine Vigan, personal communication). In our case, budesonide was unexpectedly an isolated sensitizer, with no cross-reactions to CS from the B or D groups.

The consequences of AS for the patient are largely unknown, though some authors presume it does not much affect the clinical course (5). As AS most often concerns unexpected allergens such as PPD or sesquiterpene lactones, which may be unrelated to the initial dermatoses, its consequences may generally be minor. Budesonide was a strong allergen in our patient, since dilutions down to 0.001% were still positive, as has commonly been observed in others of our patients sensitized to budesonide (unpublished data). Thus, it is likely that further skin contact with budesonide would elicit contact dermatitis.

Patch test concentrations of 1% or 0.1% pet. or eth. are recommended for budesonide, and lower concentrations of CS are thought to elicit false-negative reactions (10). However, it has been demonstrated that lower

concentrations of budesonide down to 0.0002% are able to detect contact allergy in patients negative to 0.1% (11). As the ethanolic CS mixture containing budesonide that was used during the 1st session was likely not the sensitizer, since it did not induce reaction from the 1st session, this could be an additional argument for a decrease in the standard patch test concentration of budesonide.

Acknowledgements

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Identification of new allergens and non-irritant patch test preparations

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Key words: new allergens; irritancy; false-positive patch test reactions; laser Doppler flowmetry; nickel; patch testing technique; propylene glycol; vehicles. © Munksgaard, 1998.

New allergens are identified by predictive testing and when investigating patients with contact dermatitis. A scheme used in our department is presented in Table 1. Several of the 3700 allergens listed in De Groot (1) lack or have insufficient numbers of control tests for irritancy. The number of such controls required remains a matter of debate. Fregert's (2) recommendation of 20 controls tested to a 10× higher concentration is rarely followed. An alternative might be to use the sensitive laser Doppler technique to screen test preparations for irritant potential.

Method

Test preparations were applied to healthy human volunteers for 48 h using Finn Chambers (3–5). The test sites were examined visually and measures with a laser Doppler flowmeter before, and repeatedly after, removal of the test chambers.

Results

The recommended patch test concentration for NiSO₄ is 5% (0.19 molal) and preparations in pet. and in aq. were applied for 48 h and removed one at a time. The measurements took place immediately after removal (48 h), 15 min later (48.25), and at 72 and 96 h after application. As shown in Fig. 1 there was an increase in skin blood flow, not accompanied by erythema, immediately after removal, probably due to the occlusion. This in-

crease was transient for the vehicles, and as early as 15 min, the pre-application values had been regained. For the nickel-containing preparations, the decrease was slower. NiSO₄ in pet. had a more pronounced effect on skin blood flow than NiSO₄ in aq.

Discussion

Skin blood flow must be raised 3–4× before the naked eye can detect erythema (6). Clear differences were seen when using the laser Doppler technique and comparing various water-based concentrations of propylene glycol (4) and nickel salts (sulfate, chloride, nitrate) in pet. or in aq. (5). Based on the findings and additional experience, 3 patterns of reactivity when measuring test sites can be predicted (Fig. 2). The *lower* curve is the ideal one, with only minimal and transient increase in skin blood flow. The *middle* curve is close to the threshold of visibility ("Naked eye"): with additional experiments using that particular test preparation, cases with ery-

Table 1. Scheme for identification of new contact allergens

positive patch test reaction to a product
tests with ingredients of the product
serial dilution tests to define a threshold of sensitivity
control tests for irritancy
cross-reactivity – equimolar concentrations
repeated open application tests (ROAT)

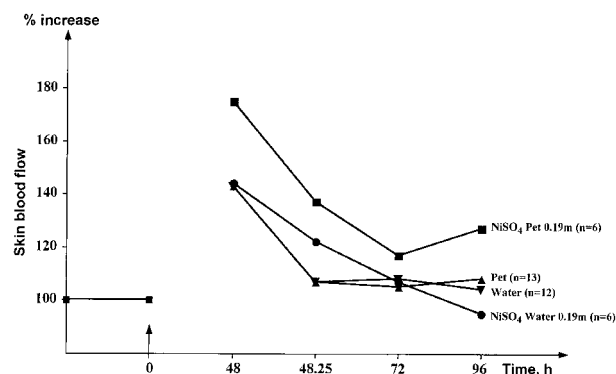


Fig. 1. Mean skin blood flow in healthy subjects before and after application of NiSO₄ in pet. and in aq. (5%; 0.19 molal), and the vehicles. The pre-application values at time 0 are set to 100%.