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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)

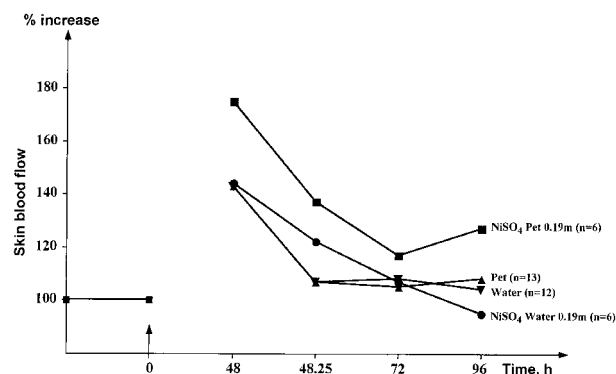


Fig. 1. Mean skin blood flow in healthy subjects before and after application of NiSO₄ in pet. and in aq. (5%; 0.19 molal), and the vehicles. The pre-application values at time 0 are set to 100%.

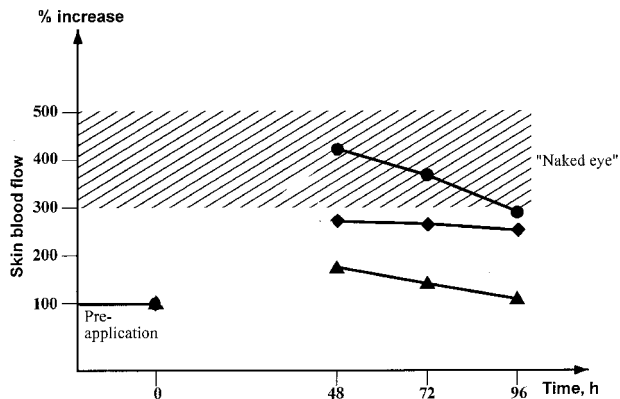


Fig. 2. Patterns of skin blood flow, when sites previously exposed to test preparations under occlusion are measured with laser Doppler flowmetry.

thema would appear. This preparation thus has a potential to be irritant on patch testing. The *upper* curve demonstrates a considerable increase in skin blood flow as well as erythema; the test preparation can be regarded as irritant and should be excluded from future use.

It can be concluded that with the laser Doppler technique, the number of controls can be reduced, and that the procedure is time-saving.

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