Comparative Multi-Center Study with TRUE Test™ and Finn Chamber® Patch Test Methods in Eight Swedish Hospitals

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292 individuals were patch tested with twelve allergens, using a new patch test technique, TRUE Test™ (TT). As controls, the same allergens in standard concentrations in petrolatum were applied using the Finn Chamber technique (FC). The allergen doses used in TT were chosen according to results from a previous serial dilution patch test study. There were reactors to all twelve allergens. The concordance of positive reactions between TT and FC was 78%. 10% were indicated only with TT and 12% FC only. Irritant reactions occurred in the same order of magnitude for the two tests. Weak positive, uncertain, and irritant reactions observed with the different test methods used, indicate minor errors of allergen dosage in both. The investigation indicates that the TRUE Test™ method is simple to handle, is well standardized and gives good accuracy with the 12 allergens investigated. *Key words: Patch testing; Contact dermatitis; TRUE Test™ Vehicle.* (Received May 1, 1987.)

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TRUE Test™ is a ready-to-use multiple patch test (1). The test has been calibrated for 12 allergens and allergen mixes in a dose–response study using a serial dilution technique (2). That study indicated similar test reactions between TT and FC with a dose ratio of about 25%. The purpose of this investigation was to confirm clinically the accuracy of the allergen dosage proposed in TT.

MATERIALS AND METHODS

The study was performed at eight different departments of occupational dermatology in Sweden during May and June 1986.

Test material

TRUE Test™ (Pharmacia AB, Uppsala, Sweden) is manufactured by incorporating allergens in different cellulose gels. A thin layer of the allergen/gel mixture is printed evenly on plastic film, dried and cut into 9×9 mm patches which are mounted on an acrylic tape (Lysapore®, Cederroths, Solna, Sweden), protected with a siliconized plastic cover and packed in a laminated, air-tight, light-impermeable envelope. Twelve different allergens and allergen mixtures are included in the first test panel.

Reference material was commercially available standard allergens in petrolatum in concentrations recommended by ICDRG (3) from Chemotechnique Diagnostics AB, Malmö, Sweden (five depart-

ments), or from Hermal Chemie, Reinbek Hamburg, West Germany (three departments). The allergens were applied with the Finn Chamber technique (Epicon OY, Helsinki, Finland). Dosage/concentrations of the panel I allergens are given in Table I.

Patients

248 patients with past or present contact dermatitis, 19 patients with other skin diseases and 25 healthy volunteers were tested, 103 men and 189 women.

All patients were Caucasians. 78% were judged to have normal skin greasiness, 5% had oily skin and 14% dry or very dry skin. 17% had mild or moderate acne on their back at the time of test application. Of the contact dermatitis group, 28% were free from dermatitis at the time of the test application, and about half had a history of hand eczema.

Test method

The two test strips, TT Panel I and the corresponding allergens in petrolatum, were applied symmetrically on the upper back. A strip with five vehicle gels served as placebo and control.

A controlled, non-blind, within-patient design was used. Patients were allocated consecutively. Left/right application varied at random.

The tests were removed at 48 h and evaluated at 72 h or 96 h.

Test readings were assessed according to the following criteria:

\- = Negative
? = Erythema, no infiltration
\+ = Erythema, infiltration, possible discrete papules
++ = Erythema, infiltration, papules, vesicles
+++ = Erythema, infiltration, coalescing vesicles
IR = Irritant reaction
P = Follicular irritation

Relevance, preference and side effects were recorded. Relevance was defined as the relation between a positive test reaction and the patient's disease. The size of positive test reactions served as a quality score.

Table I. *The dosage/concentration of the panel I allergens of TRUE Test™ (mg/cm²) and petrolatum test material (%)*

Allergens	TRUE Test™ (mg/cm²)	Concentration in petrolatum (%)
1. Nickel sulphate	0.20	2.5
2. *p*-Phenylenediamine	0.05	1
3. Neomycin sulphate	0.20	20
4. Potassium dichromate	0.025	0.5
5. Caine mix[a]	0.1+0.1+0.5	1:1:1:5
6. Fragrance mix[b]	0.08×8	2×8
7. Colophony	1.5	20
8. Epoxy resin	0.05	1
9. Thiuram mix[c]	0.006×4	0.25×4
10. Balsam of Peru	0.8	25
11. Ethylenediamine	0.05	1
12. Cobalt chloride[d]	0.05	1

[a] Dibucain, tetracain and benzocaine included in both test materials. In addition, procaine is included in the petrolatum test material.
[b] Cinnamyl alcohol, eugenol, cinnamaldehyde, α-amyl cinnamaldehyde, isoeugenol, geraniol, oak moss absolute, hydroxycitronellal.
[c] Tetramethylthiuram monosulphide, tetramethylthiuram disulphide, disulfiram, dipentamethylenthiuram disulphide.
[d] In ongoing clinical trials and in commercially available material changed to 0.02 mg/cm².

Table II. *Test result. Number of reactions TRUE Test™ (TT) and Finn Chamber method (FC)*

Allergens	TT and FC +−+++	TT: +−+++ FC: ?, IR or neg.	FC: +−+++ TT: ?, IR or neg.	TT and FC ?, IR	TT: ?, IR FC: neg.	TT: neg. FC: ?, IR
Nickel sulphate	42	1	3	3	5	4
Colophony	15	2	1	–	–	–
p-Phenylenediamine	1	–	–	–	1	1
Epoxy resin	1	1	–	–	3	1
Neomycin sulphate	1	1	2	–	1	–
Thiuram mix	8	–	1	–	–	1
Potassium dichromate	1	2	4	–	–	8
Balsam of Peru	15	4	2	–	–	3
Caine mix	3	2	2	–	1	2
Ethylenediamine	3	–	1	–	2	–
Fragrance mix	12	1	3	–	–	5
Cobalt chloride	19	2	–	5	18	1
Total	121	16	19	8	31	25

RESULT

289 patients had accurate test application. Three dropped out and are not included in the evaluation.

275 patients were evaluated at 72 h and 14 at 96 h. For each of the 12 allergens included in the test there were reactions among the tested patients. The test results are given in Table II.

In 98 individuals 156 allergens gave +−+++ reactions to one or both test methods; in 121 reaction pairs, both tests caused positive reactions, 16 were positive only to TT and 19 only to FC.

Irritation and uncertain reactions appeared equally often with either method (Table III).

Table III. *Number of irritant/follicular (IR/F) and uncertain reactions per allergen, TRUE Test™ (TT) and Finn Chamber method (FC)*

Allergen	IR/F		Uncertain reactions	
	TT	FC	TT	FC
Nickel sulphate	6	6	2	1
Colophony	–	–	2	1
p-Phenylenediamine	1	–	–	1
Epoxy resin	2	–	1	–
Neomycin sulphate	–	–	1	–
Thiuram mix	–	1	2	1
Potassium dichromate	1	8	1	2
Balsam of Peru	1	3	–	1
Caine mix	–	1	1	1
Ethylenediamine	1	–	1	–
Fragrance mix	–	2	2	5
Cobalt chloride	22	7	4	3
Total	34	28	17	16

The FC test showed statistically significant, $p<0.02$, more frequent irritant reactions to potassium dichromate, whereas with the TT method such reactions were more frequent for cobalt chloride, $p<0.001$.

There were no statistical differences in the quality scores between TT and FC tests.

Six patients demonstrated mild irritant reactions to the vehicle gels but none of them reacted to the same vehicle gel with allergen included.

A history arousing suspicion of specific contact allergy was verified by the test in only 52% of the patients. A relevant history for positive test reactions was obtained in 77% of the test—127 positive TT tests and 132 FC tests. 32 individuals had previously been patch tested with positive results, and of these 20 were TT-positive and 21 FC-positive; the remainder proved negative.

No significant preference scores were recorded; however, the investigators tend to prefer TT for the evaluation of allergy to dichromate, fragrance mix and balsam of Peru, and the control test for cobalt chloride.

Side effects

Irritation from the tape occurred in 12 TT and 18 FC tests, a non-significant difference. The tape adhesiveness was perfect in 89% of the TT tests and in 86% of the FC tests. Corners came off in most of the imperfect tests. Two TT strips and four FC strips came off completely.

No severe side effects or late reactions were reported.

DISCUSSION

There is good concordance between TRUE Test™ and the Finn Chamber method, most pronounced with strongly positive test reactions (++ and +++). Seven TT and ten FC tests of this grade were positive with a corresponding negative test. These discordant tests may represent false-negative reactions, but there may be false-positive reactions in this group too, exemplified by a FC ++ potassium dichromate test reaction which turned out to be negative on retesting.

Most weak positive reactions should be suspected of being false positives. According to an investigation into patch testing of metals, only 20% of the one-plus reactions could be reproduced as positive by retesting and thus be confirmed as allergic (4). About 40% of the present one-plus reactions were discordant with either test method (9/25 with TT and 9/22 with FC). Most of these reactions must be regarded as false positives. Discordant reactions were especially common with allergens presenting high numbers of irritant reactions, which also strengthens the assumption that they are irritant.

The reason for false-positive tests is usually a too high allergen concentration, but may also be explained by sensitive skin or an incorrect application on inflamed skin.

The discrepancies between the test results obtained by TT and FC concerning colophony and balsam of Peru may be explained by the fact that these test substances are of biological origin and that the allergens are not well defined (5, 6). It is therefore highly likely that the allergen contents of the samples differed. Preliminary tests with batches from different localities preceded the choice of test substance for TT, where the clinically most potent substance was used. Moreover, neomycin and *p*-phenylenediamine show tendencies to differ between the two test methods. The allergic reaction to these two allergens needs more time to be provoked—a 96 h evaluation would probably increase the concordance for the test methods.

Follicular reactions and uncertain reactions hardly ever indicate allergic sensitization,

but rather irritation (4). Such reactions and irritant reactions occur in the TT and FC tests in about equal numbers.

Nickel shows a tendency to irritate, with both TT and FC methods. A minor reduction in the nickel sulphate dose may be anticipated. Cobalt chloride caused a significant number of irritant, uncertain and unpaired one-plus reactions with TT, probably all irritant. Obviously the dosage of this allergen was chosen too high and is now reduced from 0.05 to 0.02 mg/cm^2. This reduction was in fact proposed already from the dose–response study (2).

Conversely, the FC tests show increased numbers of irritant reactions to potassium dichromate and fragrance mix. This indicates that the allergen concentrations of these petrolatum tests are at the irritancy limit. Previous experience has highlighted this problem (7). For this reason the potassium dichromate concentration has been reduced and fragrance mix excluded from the NACDRG (North American Contact Dermatitis Research Group) standard test panel.

The best way to determine the accuracy of a test reaction is to retest. It is interesting to note that only 60% of the patients with a previous positive test to allergens included in the TT panel were positive on retest. The reason for so many negatives may be earlier false-positive reactions, or lost hypersensitivity.

Another way to confirm the allergic background of a positive test reaction is to correlate with the patient's history. For some allergens this method is highly accurate, for others it is more doubtful. Among individuals with a history of metal dermatitis, 85–90% respond positively to nickel and/or cobalt tests. Allergic individuals are seldom unaware of their metal sensitivity, yet 10–20% of patients with positive nickel/cobalt tests, reconfirmed by retest, lack a history of metal dermatitis (8).

For other allergens, e.g. fragrances, only about half of the patients give a history that confirms the specific allergy (9, 10). This is in agreement with the present investigation, where suspicion of allergy aroused by the history could be verified in about 50% of the reactions, while post-test history verified relevance in 77% of them.

The quality of the test was defined as the area of the test reaction in relation to the area of the patch. The best quality of the test is when the reaction covers the whole area tested ±10%. A test covering less than 90% will arouse suspicion of irritancy, while more than 110% can give problems of 'spill over' effect, which may produce irritant reactions in adjacent tests. Widespread reactions are more often seen with 'petrolatum' tests than with TT, due to efflux of test material around the test, often due to an incorrect dosage (11). The TT reaction is mostly within the limits of the patch size and this must be regarded as a sign of good quality.

Patch testing implies a risk of sensitizing the patient, though small, provided that the allergen dose is adequate (12). Recently this sensitization risk has been shown to give a higher correlation with the concentration of allergen per square area than to the size of the area exposed to allergen (13). For this reason it may be an advantage to use TT with its smaller amount of allergen per area unit. Probably it is the biologically active dose rather than the amount applied that determines the risk of sensitization. Thus, an identical test reaction, indicating equivalent bioavailability, will probably also indicate equal sensitizing risk.

The allergen dosage used when patch testing is evaluated from the agreement between repeated tests with different concentrations, the absence of irritant reactions and sensitizing effects. In the comparison between TT and FC, the positive test reactions seem to correlate well, irritant reactions are mutually similar in number and no ability to sensitize has been reported. This investigation thus indicates the high quality and good accuracy of the TT test method. For most allergens, however, it is not possible from this limited study

to make a fine-graded determination of the most suitable allergen concentration. Further information of this nature will be obtained from ongoing international multi-centre studies.

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