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MODERN ACUPUNCTURE TECHNIQUES

A Double-Blind Comparison of Electrodermal Testing With Serial Dilution End-Point Titration and Skin Prick Tests for Allergy to House Dust Mite

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Abstract: This study compares skin prick testing (SPT), serial dilution end-point titration (SDEPT) and electrodermal testing (EDT) for allergy to house dust mite in 57 patients. The study was carried out in three groups of patients (A, B and C) assigned chronologically over 2-1/2 years. Our results show a high degree of correlation between SDEPT and EDT (P=0.00001). In groups A and B, a positive SPT was a good predictor of a positive EDT; this was not the case in group C. In all three groups, a positive SDEPT response predicts a positive EDT with great accuracy. The SPT is the "gold standard" for conventional allergy testing; EDT and SDEPT show a high degree of correlation with each other and a positive SPT predicts a positive EDT in 89% of instances. The implications of these results are discussed.

WE HAVE previously discussed the clinical evidence and theoretical basis of electrodermal testing (EDT).[1] Briefly, in 41 polysymptomatic allergic patients, EDT discriminated correctly 89% (average) of the time between allergens (house dust mites and histamine) and non-allergens (saline and water). It was concluded that EDT is a reliable method of differentiating between allergic and nonallergic substances. Furthermore, we also reiterated the consensus on EDT of Tiller, Smith, Munro and Benveniste[2] that a millimetric wave emission from homeopathic medications or allergens can be amplified and measured through an EDT device—a process modulated through the patient's autonomic nervous system that directly influences skin resistance.

In this second study we compare the results obtained from electrodermal testing (EDT), skin prick testing (SPT) and serial dilution end-point titration (SDEPT) for house dust mite allergy.

While there is some debate between conventional allergists and environmental physicians about the clinical value of SDEPT,[3] it is widely used within the field of environmental medicine and has become an

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Table 1.
Subjects entered into groups A, B and C

Group	Patient	Age	Gender	Diagnosis
A	1	38	F	Rhinitis
	2	25	F	Headache
	3	21	F	Irritable bowel syndrome
	4	48	F	Migraine, rhinitis
	5	48	F	Rhinitis, chronic fatigue syndrome
	6	41	M	Diabetes
	7	39	F	Migraine
	8	36	M	Asthma
	9	8	F	Asthma
	10	38	F	Irritable bowel syn., chronic fatigue syn.
	11	44	F	Headache, rhinitis
	12	11	M	Anaphylaxis, recurrent infections
	13	10	M	Asthma, recurrent infections
	14	30	F	Headache, rhinitis
	15	16	M	Headache, irritable bowel syndrome
	16	69	M	Asthma
B	1	34	M	Rhinitis
	2	28	F	Recurrent infections
	3	33	M	Recurrent infections
	4	53	F	Rhinitis
	5	9	F	Rhinitis, headache
	6	13	F	Rhinitis, chronic fatigue syndrome
	7	70	F	Asthma
	8	30	F	Asthma
	9	37	F	Rhinitis, headache
	10	49	F	Asthma
	11	49	M	Rhinitis, chronic fatigue syndrome
	12	11	F	Asthma
	13	41	F	Chronic sinusitis
	14	62	F	Tachycardia
	15	27	F	Rhinitis
	16	28	F	Asthma
	17	45	F	Rhinitis, fibromyalgia
C	1	36	F	Rhinitis
	2	19	M	Migraine
	3	52	F	Rhinitis, irritable bowel syndrome
	4	56	F	Migraine, rhinitis
	5	32	F	Rhinitis
	6	49	F	Premenstrual syndrome, rhinitis
	7	36	M	Irritable bowel syndrome, rhinitis
	8	38	F	Asthma, headache
	9	32	M	Urticaria
	10	6	M	Sinusitis
	11	47	F	Migraine, rhinitis
	12	53	F	Migraine, rhinitis
	13	49	F	Asthma
	14	47	F	Irritable bowel syndrome, rhinitis
	15	53	F	Chronic cystitis
	16	58	M	Asthma
	17	28	F	Irritable bowel syndrome, migraine
	18	47	M	Migraine, rhinitis
	19	67	M	Irritable bowel syndrome, asthma
	20	11	F	Urticaria, irritable bowel syndrome
	21	15	M	Asthma
	22	40	F	Migraine
	23	41	M	Asthma
	24	43	F	Irritable bowel syndrome

pted technique by many doctors practicing within this area.[4] The Position Paper of the Canadian Society for Clinical Ecology and Environmental Medicine[5] also makes it quite clear that SDEPT is a fundamental part of the practice of environmental medicine, and furthermore considers SDEPT well validated as a diagnostic method in allergic disease, in the context of properly constructed randomized, controlled trials.

Skin prick testing is widely used diagnostically in allergy practice and almost certainly measures IgE mediated allergic reactions to substances such as pollen, molds and animal dander.[6] However, the use of skin prick testing to evaluate food allergies or intolerance is both inaccurate and unreliable.[7]

SDEPT measures not only IgE mediated reactions as shown by skin response, but may also involve other mediators such as IgG and perhaps other unknown and as yet escribed mechanisms.[8] Not only may it .. uce skin reaction at the site of injection in sensitive individuals, but it may also induce a variety of systemic symptoms, often triggering, quite aggressively, symptoms usually caused by the allergic substance.[8]

As a consequence, we deemed it reasonable to compare an unconventional and largely untested form of allergy testing, EDT, with SDEPT, utilized by most physicians practicing within the field of environmental medicine, and with SPT as the primary conventional method for allergy testing for house dust mite.

Aim

To compare EDT with SDEPT and SPT for diagnostic efficacy involving dust mite allergy, in a double-blind, randomized, controlled manner, in patients attending an environmental medicine clinic with multisystem complaints.

Materials and Methods

Subjects

Fifty-seven patients, 39 females and 18 males, ranging in age from 6-70 years, with a variety of symptoms and illnesses (see Table 1) were chronologically entered into three study groups (A, B and C) while attending the medical office of a physician with a special interest in environmental medicine (author JK). The study period extended over 2-1/2 years, during which time new patients were added, as circumstances and time permitted during a regular clinical practice; a new group would be started after an interruption (e.g., 6 months).

Informed consent was obtained from all study subjects.

Group A had 16 patients, Group B had 17 patients, and Group C had 24 patients. There were no obvious differences between the three groups in relation to their age, gender and main diagnosis.

Patients were excluded from the study if they were less than 6 or greater than 70 years of age, had been tested previously for mites by skin prick test or SDEPT, had been previously treated for mite allergy, had a negative histamine prick test, or were taking antihistamines or tricyclic antidepressants.

All patients gave a full medical history, were given a physical examination and various standard laboratory blood tests as indicated by their condition. All had multisystem disorders. The majority gave a medical history of present or past symptoms of allergy causing rhinitis or asthma.

All patients were first tested with a Vegatest II,[9(p19),10] followed by the allergy skin prick test[11] at the same office visit. The SDEPT procedure[5,12] was usually done within 10-14 days. Each test was done only once.

Electrodermal Testing Procedure

We used a Vegatest II (Vega Grieshaber GmbH & Co, Schiltach, Germany) device for

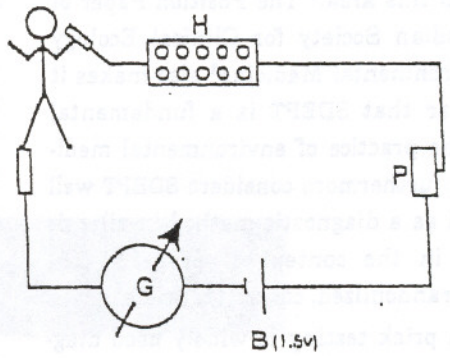

Figure 1.
Schematic diagram of current circuit in Vegatest II setup:
H = honeycomb; G = galvanometer; B = battery; P = point regulator

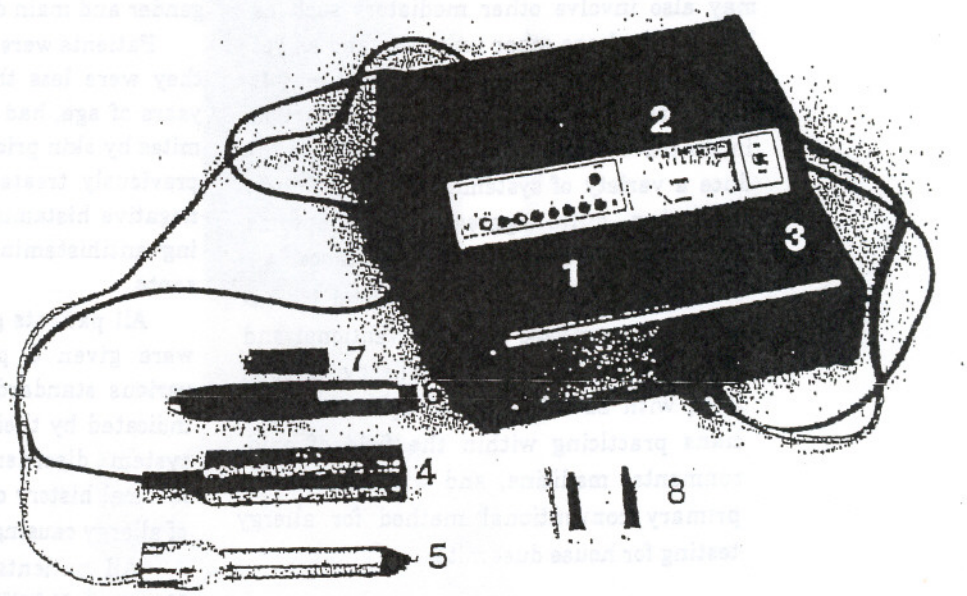

Figure 2.
Vegatest II device and accessories

1. Honeycomb
2. Reading scale
4. Point regulator
4. Silver electrode
5. Measuring stylus
6. Stimulator
7. Cadmium battery for "disorder control"
8. Ampule of Ferrum Metalliicum 12x
9. Ampule of Manganum 30x

EDT testing. The schematic diagram for the Vegatest II and a description of the testing procedure is provided in the manufacturer's manual[9(p19)]; and has been described previously.[10] A simplified schematic representation of the Vegatest II device is shown in Figure 1; here the potential difference between the honeycomb (H) containing an antigen to be tested and an acupuncture point of the patient is monitored by galvanometer (G).

The Vegatest II galvanometer is connected in a closed circuit with the honeycomb and accessory devices (see Figure 2). The first connective tissue point [Voll's control measurement point: Fibroid and Interstitial Degeneration (FibD1)][9(p14)] on the medial side of the third toe is routinely used in EDT measurements. The use of this particular acupuncture point is a standard part of the Vega protocol, but has never been critically evaluated.[9(p14)] A measurement stylus is used at the selected point and the 'nt regulator is tuned (decreased or in-.eased in intensity) until the maximum 100 scale unit (SU) value is reached. In order to determine that the machine is properly tuned to the patient, an ampule of a "disordering substance," e.g., a heavy metal such as cadmium (a used battery), is introduced into the machine's honeycomb. The measurement indicator should then show a lower reading of 50-60 SU.

Next, the sealed glass ampule containing the concentrate of the antigen to be tested is placed into the honeycomb together with the homeopathic filter Ferrum Metallicum[9(p14),13] in a dilution of D12. The indicator of the galvanometer will show a low reading of 50-60 SU if the patient is sensitive. If the patient is not sensitive, the galvanometer will show a high reading of 100 SU.

Two identical sets of four different substances (water, saline, histamine and house dust mite) contained in identically-shaped glass ampules were blinded by an independent researcher for our EDT testing.

Originally, only one sample set of ampules (blinded and coded by numbers) was used in the first group of patients (Group A). Later, in Groups B and C it was decided to improve the study and add the second sample set of blinded ampules that were coded by letters. Thus, Groups B and C were tested with two sets of blinded ampules, those with numbers and those with letters.

In all groups (A, B and C) the coded and sealed glass ampules were tested on the same patient on the same day by a technician who did not know the contents of either set, and each solution was tested randomly.

The technician was in each instance asked to identify the ampules showing an allergic response (reading 50-60SU) by recording a plus (+). The blinding code was broken at the end of the experiment; the ampules identified correctly were marked "+"; and incorrectly, "–" (see Tables 2 and 3).

SDEPT Testing Procedure

SDEPT was performed by an experienced technician using a 1:5 serial dilution technique.[4] A concentrate of house dust mites, using a mixture of *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* from Bencard Allergy Laboratories (Mississauga, Ontario, Canada), at a strength of 1% was diluted serially with a coca solution (2% normal saline, 0.5% sodium bicarbonate) by a factor of five. A specific amount (0.01cc) of the test antigen (mites) dilution was injected intradermally to form a measurable wheal (usually 4mm) which was observed for any significant change. When increasing concentrations of antigen were applied, a progressive whealing response was produced. The test was considered positive if, after 10 minutes following injection, the wheal grew two or more millimeters or there were systemic symptoms. The

Table 2.

Group A: Comparison of SPT, SDEPT and EDT in patients sensitive to dust mites*

Patient	Age	Gender	SPT	SDEPT	EDT
1	38	F	+	+	+
2	25	F	+	+	+
3	21	F	+	+	+
4	48	F	-	+	+
5	48	F	+	+	+
6	41	M	+	+	+
7	39	F	-	+	+
8	36	M	-	+	+
9	8	F	+	+	+
10	38	F	+	+	+
11	44	F	-	+	+
12	11	M	+	+	+
13	10	M	+	+	+
14	30	F	-	+	+
15	16	M	+	+	+
16	69	M	+	+	+

* Test ampule identification: + Correct response; - Incorrect response

Table 3.

Groups B & C: Comparison of SPT, SDEPT and EDT in patients sensitive to dust mites*
(EDT number & EDT letter = codes for 2 sets of identical & blinded samples of mite antigen)

Group	Patient	Age	Gender	SPT	SDEPT	EDT#	EDT letter
B	1	34	M	+	+	+	+
	2	28	F	+	+	-	-
	3	33	M	-	+	+	-
	4	53	F	+	+	+	+
	5	9	F	+	+	+	+
	6	13	F	-	+	+	+
	7	70	F	+	+	+	-
	8	30	F	+	+	-	+
	9	37	F	+	+	+	+
	10	49	F	+	+	+	+
	11	49	M	-	+	+	+
	12	11	F	+	+	-	-
	13	41	F	-	+	+	+
	14	62	F	+	+	-	-
	15	27	F	-	+	+	+
	16	28	F	+	+	+	+
	17	45	F	-	+	-	-
C	1	36	F	-	+	+	+
	2	19	M	-	+	+	+
	3	52	F	+	+	+	+
	4	56	F	-	+	+	+
	5	32	F	-	+	+	+
	6	49	F	-	+	+	+
	7	36	M	-	+	+	+
	8	38	F	+	+	+	+
	9	32	M	-	+	+	+
	10	6	M	-	+	+	+
	11	47	F	-	+	+	+
	12	53	F	-	+	+	+
	13	49	F	+	+	+	+
	14	47	F	-	+	+	+
	15	53	F	+	+	+	+
	16	58	M	-	+	+	+
	17	28	F	+	+	+	+
	18	47	M	-	+	+	+
	19	67	M	-	+	+	+
	20	11	F	-	+	+	+
	21	15	M	-	+	+	+
	22	40	F	-	+	+	+
	23	41	M	-	+	+	+
	24	43	F	+	+	+	+

* Test ampule identification: + Correct response; - Incorrect response

...st was considered negative if there was no growth of the wheal in response to dilution No 1 (a 1:5 dilution).

Skin Prick Testing Procedure

The standard skin prick test for the same antigen (Bencard Allergy Laboratory house dust mite mixture) was carried out blind, with the mites being one of several antigens tested; the procedure was performed exactly as described previously.[11]

Control Procedures

A negative control test for normal saline and a positive control test for histamine were performed before both the SDEPT and skin prick tests. These tests were performed independently by each technician and there was no communication between the technicians regarding the results. Vega testing was performed first in order to avoid skin contact with the antigen used in the prick test or SDEPT methods.

...atistical Evaluation

Statistical analysis was performed with the assistance of Laurel Trainor, PhD and Professor Rolfe Morrison, both from the Department of Psychology at McMaster University in Hamilton, Ontario and Dr. Lorraine Low at the Department of Medical Statistics and Computing, University of Southampton, Hampshire, England. In addition to using Fisher's exact test to define the correlation between SPT, EDT and SDEPT, a Kappa coefficient was also calculated to evaluate chance-corrected proportional agreement When considering a Kappa coefficient, a value of <0.2 represents poor agreement, 0.21-0.4 fair agreement, 0.41-0.6 moderate agreement, 0.6-0.8 good agreement and 0.81-1.0 very good agreement.

Results

All three groups were SDEPT and EDT positive in 93% of instances. However, when comparing both SDEPT and EDT to SPT, differences do emerge. Groups A and B were skin prick positive in 69% and 65% of instances respectively, but in Group C only 25% were SPT positive. In Groups A and C, all 17 patients with a positive SPT also had a positive EDT. However, in Group B, 11 patients had a positive SPT, three of which did not show any positive reaction on EDT. In total, therefore, of 28 patients with a positive SPT, all but 3 also had a positive EDT; therefore in 89% of our patients in this study, a positive SPT predicts a positive EDT. SPT results show Groups A and B combined to be substantially different from Group C: 67% positive SPT (A plus B) versus 25% (C) positive SPT (P=0.01 Fisher's exact test).

Tables 2 and 3 show that SDEPT and EDT correlate significantly (P=0.00001, Fisher's exact test). In Groups B and C (Table 3), EDT was tested twice using identical blinded samples of antigen. Overall, there was 93% concordance between the 57 patients in this study when comparing SDEPT and EDT. There was, however, a substantial difference between SPT and both SDEPT and EDT, as shown in Tables 2 and 3.

The Kappa coefficient provides us with further information in relation to these three methods of allergy testing. When EDT was compared to SPT in group A, a positive SPT was able to predict with good agreement a positive EDT (Kappa coefficient 0.69). The Kappa coefficient when comparing EDT and SDEPT in group A was 1.0; a positive SDEPT therefore has an excellent predictive value for a positive EDT (see Table 2).

In group B, a positive SPT predicted positive EDT with a Kappa coefficient of 0.58 in relation to EDT-number coded tests, and 0.64 in relation to EDT-letter coded tests, again a good predictive value overall. In group B, a positive SDEPT predicts a positive EDT with a Kappa coefficient of 1.0, for

both sets of test ampules, i.e., coded by number and by letter (see Table 3).

Group C shows very poor correlation between SPT and EDT. A positive SPT predicts a positive EDT with a Kappa coefficient of 0.25 both for EDT-number and EDT-letter. However, the predictive value of a positive SDEPT showing a positive EDT was again 1.0 for both EDT-number and EDT-letter tests (see Table 3).

Discussion

The skin prick test is regarded as the gold standard for IgE mediated allergies such as dust mite, pollens and animal dander. It is clear that in the first two groups of patients (A and B) a positive SPT was considered a good, but not infallible, predictor of a positive EDT. This was not the case in Group C (25% positive SPT versus 100% positive EDT). Table 1 suggests that there was little obvious difference between the patient groups, in terms of age, gender and underlying diagnosis; however, patient characteristics, diet, and seasonal variation during which testing occurred and other environmental factors could have contributed to this difference. It is difficult to explain the disparity between Groups A + B and C with respect to skin prick testing; perhaps chance is the most important unknown factor. However, we must consider other explanations such as the possibility that SPT is measuring substantially different aspects of allergy when compared to SDEPT or EDT. It is also possible that the results obtained from both EDT and SDEPT involve substantial artifact in association with many false positive tests.

However, it is quite unlikely since in our previous study,[1] EDT was able to differentiate both reliably and accurately between sealed ampules of house dust mite/-histamine (allergic substances) and sealed ampules of saline/water (non-allergic substances). In view of those results, it is difficult to argue that EDT is entirely valueless or is associated with substantial occurrences of false positive results.

Clinical trials involving SDEPT have been reviewed previously.[3,4] As suggested in our introduction, and on the basis of over 35 double-blind, randomized, controlled trials, it would appear that SDEPT is considered a reliable technique in the diagnosis of allergies and can also be used as the basis for provoking and neutralizing symptoms in polysymptomatic patients who may be thought of as having multiple allergies.[8] Therefore, it is unlikely that SDEPT is as prone to artifact as a negative interpretation of these results might suggest. Those practicing environmental medicine have found that the technique of SDEPT has provided them with valuable clinical information as to a patient's allergic status. As a consequence, most environmental physicians will tend to use SDEPT as their gold standard, unlike the more conventional allergists, who would consider SPT their gold standard.

Furthermore, Leipzig and Slavin[6] state: "Intradermal tests (such as SDEPT) are more reproducible than epicutaneous tests (such as SPT) being 100 to 1000 times more sensitive. Thus, they are associated with fewer false-negative reactions." Demoly, Bousquet and Manderscheid[7] have shown that different techniques and pricking devices contribute from 10-30% variability in SPT in routine clinical practice. There is unpredictability associated with SPT since an exact amount of antigen cannot accurately be introduced into the skin. On the other hand, SDEPT demands a far more accurate dosage and injection protocol and one can therefore speculate that the results obtained may possibly be more accurate and reproducible.

It is clear from both this study and our previous paper that EDT reliably differenti-

ates between allergic and non-allergic substances and is significantly concordant with SDEPT.[1,10] Tsuei came to similar conclusions about the correlation between EDT and SDEPT when evaluating SDEPT using the Dermatron EDT apparatus.[14] Ali[15] found that electrodermal testing using the Interro apparatus was comparable with specific IgE antibodies using the micro ELISA procedure in 73% of patients allergic to pollens and molds. Our findings further support the observation that SDEPT and EDT may be measuring similar components of allergy.

More research is required to understand the underlying mechanisms involved in both tests (particularly the ability to provoke symptoms during SDEPT), involvement of the autonomic nervous system in EDT, and their possible interaction. This assumption presently remains a hypothesis related to the field of psychoneuroimmunology and supported by clinical observation.

It would therefore be logical for us to suggest that SPT and SDEPT look at different aspects of the allergic mechanism, but that both may have an important clinical value. It is also reasonable to suggest that SDEPT and EDT may be measuring similar aspects of allergy. When taking the whole picture into account in relation to these two tests (SDEPT and EDT), it appears unlikely that we are simply looking at false positive tests, but rather that we are looking at different aspects of allergy that are not routinely evaluated in conventional medicine. We can conclude from this and our previous study[1] that it is quite possible to use SDEPT and EDT interchangeably in the investigation of an individual's allergic status and correlate it with the clinical history and total picture of the patient.

This study would benefit from repetition, comparing a variety of different allergy tests in a more closely defined group of patients; ideally these patients should have one allergic condition such as asthma or eczema. Because this study was carried out in the context of a busy clinical practice it was not possible to insert adequate controls. Repetition of this study should take this into account and, therefore, the study should not only be more focused in its methodology, but also in the controls used, so that outcomes can be evaluated more clearly.

In Sum

We conclude that EDT can be used alone or in conjunction with other tests such as SPT, SDEPT, RAST, etc. Electrodermal testing is:

1. Very time efficient
2. Easy to perform once the technique is learned
3. Reliable
4. Objective
5. Cost-effective
6. Useful for patients who are exquisitely sensitive, incompetent or unable to cooperate, including infants.

Acknowledgements

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