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CRITICAL STUDY OF THE SPECIFICITY OF THE SKIN-WINDOW TEST IN ALLERGY

By

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The skin-window test (S.W.T.) is a biological method developed and used for the first time by *Rebuck & Crowley*, for the study of inflammation. Afterwards it was used by other workers such as *Archer, Cole, Eidinger, Wilkinson & Rose, Fowler & Lowel, Feinberg & Feinberg, Wolf-Jürgensen* for the study of inflammation during an allergic reaction. Some have applied histamine itself, others specific Antigen (Ag). They have shown that a positive reaction should produce a tissue eosinophilia.

The present work aims at elucidating the value of the skin-window test concerning its specificity in relation to the Intra-dermal (I.D.) test and its probable practical use in clinical allergy.

METHOD AND MATERIAL

We have applied 116 skin-window-tests (S.W.T.) on 86 adult male and female patients, either day-patients or patients from the hypoallergy wards. They almost all showed a polyvalent reactivity to the intra-dermal (I.D.) reactions.

The Antigen (Ag) had previously shown a positive I.D. reaction in the same patient except in the cases of drug allergy in which only the history indicated the substance to be tested. We tried to improve the method by using a derma-brasion apparatus which produces a smooth abrasion of the same depth along the whole surface. The exudate was rich and homogeneous and we counted at least 300 cells and in some cases up to 1,000 cells.

The slides were read every 2, 4, 6, 24, and 48 hours. The Ag used were pollens, house dust, candida, moulds, and drugs, *i.e.* antigens of different

chemical nature and antigenicity, divided into 3 large groups according to these properties.

- I. Pure protein antigens, of great antigenicity – pollens
- II. Complex protein – antigens with a large proportion of protein
 - a) house dust
 - b) candida
 - c) moulds
- III. Haptenic antigens – drugs

A skin-window test was considered positive if it showed a tissue eosinophilia 3 per cent higher than that of the control, bearing in mind that a blood eosinophilia is normally up to 3 per cent. A blood eosinophilic count was usually made although this examination in our opinion is not necessary as blood does not come to the surface if the abrasion is correctly performed.

RESULTS

Group I – Pollen

This group contained 10 patients, suffering from asthma and/or rhinitis with a positive scratch test to pollens. The dilutions used for the S.W.T. were 10 to 100 times greater than those which gave a positive scratch test. All our patients developed a tissue eosinophilia from 4–40 per cent. One patient with a doubtful scratch test had a 2 per cent tissue eosinophilia, so a doubtful S.W.T. too. Another patient showed no eosinophilia in S.W.T. 48 hours after using the method of quadrillage desensitization.

The first patient was considered the group control, the second a demonstration of the refractory period after a desensitization. She had a very intense reaction to the quadrillage.

Group II

A. House Dust. – 26 S.W.T. were performed on 22 patients. 11 S.W.T.s on 10 of these patients showed tissue eosinophilia from 6–42 per cent. The dilutions used were 1:50, 1:500, 1:5,000. The 11 S.W.T.s with eosinophilia were distributed in the following way:

- 4 S.W.T.s on 6 patients with a positive I.D. test to 1:5,000,000
- 3 S.W.T.s on 7 patients with a positive I.D. test to 1:500,000
- 4 S.W.T.s on 8 patients with a positive I.D. test to 1:50,000

Of these patients 5 with a negative S.W.T. and 4 with a positive S.W.T. were under specific desensitization. A patient with a positive I.D. reaction to 1:5,000 gave a negative S.W.T. and was considered the group control.

B. Candida. — 18 S.W.T.s were performed on 11 patients. 8 S.W.T.s on 5 patients showed tissue eosinophilia. The dilutions used were 1:100, 1:1,000, 1:10,000.

The S.W.T. with eosinophilia were distributed in the following way:

- 2 S.W.T.s on 2 patients with positive I.D. to 1:100,000
- 1 S.W.T.s on 5 patients with positive I.D. to 1:10,000
- 2 S.W.T.s on 4 patients with positive I.D. to 1:1,000

C. Moulds. — On 14 patients, 29 S.W.T.s were performed and only 3 patients had a positive S.W.T. with an eosinophilia from 3–50 per cent. 3 patients with a negative S.W.T. were under desensitization towards dust and also on steroid therapy. The dilutions used were 1:100 for the I.D. reactions on all the patients and 1:10, 1:100, 1:1,000 for the S.W.T. of moulds-mixture I, II, III, IV depending on the mixture that gave a positive I.D. test.

Group III

Drugs. 26 S.W.T.s on 23 patients were performed and only 7 S.W.T.s had a positive eosinophilia from 3–33 per cent.

CONCLUSIONS

On 86 patients 116 S.W.T.s were performed and 45 showed a tissue eosinophilia (Fig. 1) in comparison to the S.W.T. control with isotonic Saline. The S.W.T. with eosinophilia

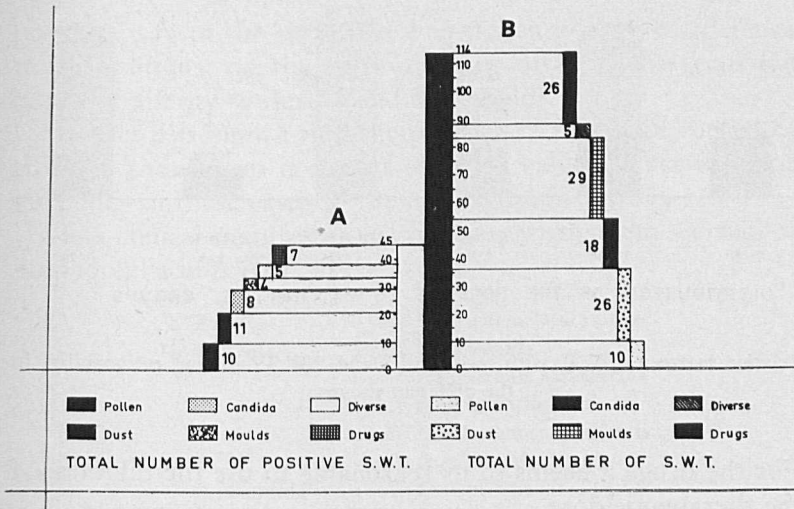


Fig. 1.

- A) Numbers of S.W.T. with eosinophilia per group, contributing to the total number of S.W.T. with eosinophilia.
- B) Contribution of the numbers of S.W.T. with a given Ag to the total number of S.W.T. performed.

were distributed in a different way in 3 groups according to the chemical nature and the antigenicity of the Ag (Fig. 2).

- I. Pollen – 10 S.W.T.s positive to 10 S.W.T. applied (100 %)
- II. A. Dust – 11 S.W.T.s positive to 26 S.W.T. applied (42.3 %)
- B. Candida – 8 S.W.T.s positive to 18 S.W.T. applied (44.4 %)
- C. Moulds – 4 S.W.T.s positive to 29 S.W.T. applied (13.7 %)
- III. Drugs – 7 S.W.T.s positive to 26 S.W.T. applied (26.9 %)

The dilutions used of the different Ags seem to be important for the appearance of the tissue eosinophilia. We used when possible 2–3 dilutions of the same Ag and it was confirmed that the convenient dilutions are for the dust 1:50, 1:500, for Candida 1:1.000 or 1:10.000 and 1:100 for moulds.

Concerning the pollens the dilution used was 10 to 100 times greater than that which gave a positive scratch test.

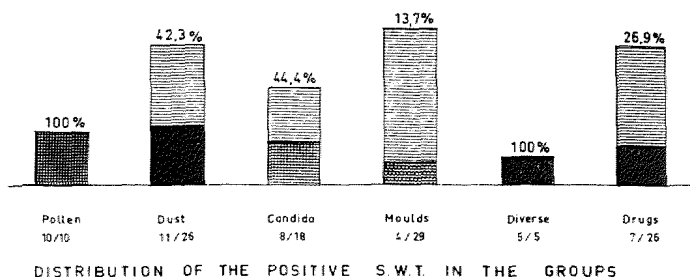


Fig. 2.

Relation between S.W.T. with eosinophilia and S.W.T. without eosinophilia in the different groups.

For the drugs it seems to us reasonable to use the dilution of the therapeutic dose.

It seems that the frequency of the appearance of tissue eosinophilia depends on the patients' sensitivity and consequently titre of circulating antibodies, while we are cautious about the specificity of the positive I.D. reactions.

In the group of dust:

- In 6 patients with positive I.D. test to 1 : 5,000,000
4 presented tissue eosinophilia
- In 7 patients with positive I.D. test to 1 : 500,000
3 presented tissue eosinophilia
- In 8 patients with positive I.D. test to 1 : 50,000
4 presented tissue eosinophilia

In the group of Candida:

- In 2 patients with positive I.D. test to 1 : 100,000
both showed tissue eosinophilia
- In 5 patients with positive I.D. test to 1 : 10,000
1 showed tissue eosinophilia
- In 4 patients with positive I.D. test to 1 : 1,000
2 showed tissue eosinophilia

In the group of moulds, the results are too few to draw a conclusion.

Thus it is observed that the S.W.T. which is positive in a

parallel way to the scratch test in pollen allergy with clinical manifestations, on the contrary very often is dissociated in cases of allergy to dust, *Candida*, moulds. —

In fact it is known that the positive I.D. in high concentrations in these cases is not of constant value, a fact that corresponds in these cases to the negativity of S.W.T.

The clinical manifestations of the patients who showed an eosinophilia in S.W.T. are :

I. Pollen —	10 suff. from asthma and rhinitis
II. A. Dust —	4 suff. from asthma
	2 suff. from asthma and eczema
	1 suff. from Quincke's oedema
	3 suff. from asthma and rhinitis
	1 suff. from rhinitis
B. <i>Candida</i> —	2 suff. from asthma
	3 suff. from Quincke's oedema
C. Moulds —	2 suff. from asthma
	1 suff. from urticaria and Quincke's oedema
III. Drugs —	1 suff. from urticaria-antipyrine
	1 suff. from rhinitis-aspirine
	1 suff. from spastic cough-sultrène
	1 suff. from urticaria-quinine
	1 suff. from face oedema-desomedine
	1 suff. from erythema Barbiturate
	1 suff. from fixed eruption Barbiturate
	1 suff. from urticaria-streptomycine
	1 suff. from urticaria-penicillin
	1 suff. from urticaria-epidione

So, one can see that the clinical manifestations of the patients who showed a tissue eosinophilia are of the immediate type *i.e.* characterised by circulating antibodies, even in the group of drug allergy.

Atopy, that is to say the familial tendency to be easily sensitized seems not to be very frequent among our patients who gave a positive I.D. test, neither was it necessary among those who presented a tissue eosinophilia. Of course the atopy was detected only by the history and questioning the patients a fact that does not exclude a latent atopy. It appears in the groups in the following way.

	<i>Positive I.D. reaction</i>		<i>S.W.T. with eosinophilia</i>	
	No. of patients	Atopy	No. of patients	Atopy
Pollen	10	5	10	5
Dust	22	5	11	4
Candida	12	0	5	0
Moulds	14	1	3	0
Drugs	29	6	7	1
	87	17 (19.5%)	36	10 (27.7%)

DISCUSSION

Recent studies by various workers have shown that the eosinophilia is induced by the complex Antigen + Antibody (Ab) (2, 3, 7, 11, 15, 16) of a certain configuration (11) and that histamine potentiates but does not induce eosinophilia (1, 7). This theory is supported by our study in which from 86 patients with positive I.D. test, 17 stated that they were atopic and among those only 10 showed tissue eosinophilia a fact that makes one think that histamine does not precipitate tissue eosinophilia, if an Ag + Ab complex does not exist even in atopic patients who are supposed to show an easy histamine release and an increased sensitivity toward it and who present a positive I.D. test.

The clinical manifestations of the patients who showed a tissue eosinophilia are of the immediate type and consequently characterized by circulating Abs (complete). The fact that S.W.T.s with eosinophilia are distributed in a different way in the 3 groups studied, seems to be related to the chemical nature and the antigenicity of the Ag tested. Pollens (almost pure protein and of great antigenicity) produce a tissue eosinophilia in all cases; on the contrary in the second group, in which the chemical nature of the Ag is complex and of weak antigenicity, the appearance of eosinophilia is not constant in a S.W.T. with the Ag which induces a positive I.D. reaction. In

the group of drug allergy where we are dealing with haptens it is even more seldom.

It is therefore concluded that the chemical nature and the antigenicity of an Ag, which is responsible for the production of different kinds of Abs, induce tissue eosinophilia if they produce a complete Ab (1). The explanation of a positive I.D. test to an Ag which did not induce tissue eosinophilia in the S.W.T. does not seem to us difficult. It is known that the I.D. reaction is a Lewis reaction due to histamine which may be released specifically (Ag + Ab reaction) or non-specifically from the skin trauma and the introduction of a foreign substance. One may think also that it may be due to incomplete Abs which can produce oedema but not eosinophilia (1). If we accept the results of the work of other research workers on eosinophilia, it seems that the S.W.T. could be used to differentiate a true positive I.D. reaction from a false positive one and can be used consequently as an exposure test especially before undertaking specific desensitization.

SUMMARY

In 86 patients, 116 Skin Window Tests (S.W.T.) were performed and 45 showed a tissue eosinophilia often associated with a basophilia. The positive S.W. Tests are distributed in a different way in the 3 main groups of the study. The tissue eosinophilia seems to be controlled by the chemical nature, the antigenicity and the dilution of the antigen (Ag) used. In the group in which the Ag is a pure protein, the S.W.T. is 100 per cent positive (10/10). In the group in which the Ag is a complex substance and in which the protein part is small, the percentage of S.W.T. with eosinophilia varies. It is less than half in the group of dusts and *Candida* and even less in the group of moulds and drug allergy. The dilutions to be used seem to be very important. For the pollen group, must be 10–100 times higher than that which gave a positive scratch test.

In the other groups the concentration 1:500 for the dust,

1:1,000 or 1:10,000 for *Candida* and 1:100 for moulds seems to be convenient.

The skin-window test seems to be of great specificity and sensitivity and can be used as an exposure test to verify the specificity of a positive intradermal test especially before starting desensitization. Its value in drug allergy, remains doubtful especially if one wishes to exclude an immune mechanism after a S.W.T. without eosinophilia.

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