ROUTINE PATCH TESTING V*

Correlations of Reactions to the Site of Dermatitis and the History of the Patient

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The Scandinavian Committee for Standardization of Patch Testing was established in 1962 with the aim of selecting a number of substances suitable for a standard patch test series in the Nordic countries (2). In previous papers the Committee has described the study, which comprised substances applied with identical patch testing techniques (3, 4, 5). Pooling of the results indicated that although the incidence of reactions to the individual substances varies, the twenty most common allergens were the same in Denmark, Finland, Norway and Sweden.

The incidence of sensitivity to some substances, such as chromium, neomycin and turpentine, showed, however, considerable variation from one hospital to another. Such differences might reflect unlike allergenic environments, but they might also be dependent on the selection of patients. It soon became apparent that the differences in the sensitivity established among male and female patients at one hospital were greater than differences in total results between the individual countries. In addition to sex, other factors, such as the age of the patients, and the types and prevailing localization of dermatitis also influence the results of standard patch tests in different series of patients tested.

In the present study we have extended our previous work by including an analysis of the clinical relevance of the positive reactions and the occurrence of multiple sensitivities. At the same time, however, the material serves to illustrate the extent of important differences in the selection of patients for testing, which may account for some of the differences in the incidence of sensitivities previously reported.

Material and Methods

The study comprised 1027 consecutive patients seen during the same period of time at the five participating hospitals. As described in previous papers the indications for patch testing differ slightly from one hospital to the other.

On the basis of previous studies the six substances which most commonly gave positive reactions were included in the present study (Table 1). "Aluminium" test (Fregert) (6) was used for test patches, Leucoplast^{®1} adhesive tape for fixation of patch tests at the upper back. The patches were left for 48 hours, and the reactions were read at removal and one day later.

The routine series used at the various clinics differed in details but had the same basic substances (5). The test results with

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Table 1. Distribution (%) of the test results with the six most common allergens according to sex of the patient. 1027 patients tested at five hospitals

	418	males	609 females					
	Mean (%)	Range (%)	Mean (%)	Range (%)				
Potassium dichromate (0.5 % aqueous)	10	7-12	2	1-3				
Nickel sulphate (5% aqueous)	4	1–6	8	4-10				
Formaldehyde (2 % aqueous)	4	0-8	5	3-10				
p-Phenylenediamine (2 % in petrolatum)	5	2-9	7	2-10				
Balsam of Peru (25 % in petrolatum)	9	4-24	12	5-22				
Neomycin sulphate (40 % in petrolatum)	4	1–8	4	0-11				

Table 2. Summary of factors which might influence the incidence of routine patch test reactions

	418 n	nales	609 females						
	Mean (%)	Range (%) in 5 hospitals	Mean (%)	Range (%) in 5 hospitals					
Sex	41	31-58	59	42-69					
Domestic work only	1	0-2	38	26-53					
Atopic dermatitis	8	4-12	8	4-15					
Site of dermatitis									
Hand	66	54-79	57	20-69					
Foot	20	10-29	9	6-11					
Lower leg	20	14-24	15	8-30					
Other site	42	35-58	44	33-64					

six of these (dichromate, nickel sulphate, formaldehyde, p-phenylenediamine, balsam of Peru and neomycin sulphate) and some clinical data were noted on a special form (Fig. 1). In order to determine the total number of patients with positive reactions, the results of other patch tests were also marked on the form. Multiple sensitivity was marked if a reaction to two substances, not known to cross-sensitize, was found.

For collation of the data and determination of correlations a Card sorter IBM 83, Collator IBM 88 and an Accounting Machine IBM 444 were used.*

Results

The results of patch testing with the small series confirmed previous findings that balsam of Peru was the most common allergen in the total series and among the females, but surpassed by chromium sensitivity among the males (Table 1).

Table 2 gives a summary of factors expected to have an influence on sensitivities found in a particular hospital. 59 per cent of the total material were females and 38% of the females had domestic work only.

The difference in the incidence of hand dermatitis may determine some of the dif-

² The Data Center, County Council, Lund, Sweden. 37 - 337-5619. Acta Derm. 49:6

Name: Record No.: Hospital: Bergen = 1, Gothenburg Sex: (male = 1, female = 2) Domestic work only: (yes = 1, no Atopic dermatitis: (yes = 1, no = 2)	= 2)	Lund = 4, Stockholm = 5	0000
Localization		Hand Foot Lower leg Other sites	0000
Test reaction: (Positive = 1, negati	ve = 0)	Dichromate Nickel sulphate Formaldehyde p-Phenylenediamine Balsam of Peru Neomycin sulphate	000000
Connection of test-reactions to pro (No = o, yes = 1)	esent dermatitis	Dichromate Nickel sulphate Formaldehyde p-Phenylenediamine Balsam of Peru Neomycin sulphate	000000
Reaction to other substance(s); (Reaction to other substance(s); (Multiple sensitivities (yes = 1, no	Pos. = I , neg. = O) no		000

Fig. 1. Form used for case notes.

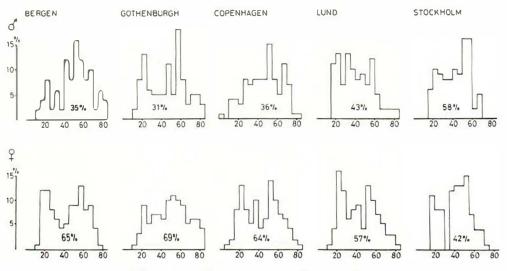


Fig. 2. Age and sex distribution in five hospitals.

Table 3. Percentage of positive patch test reactions considered relevant to the present outbreak of dermatitis (1027 patients at five hospitals)

Test substance	418 males	609 female:		
Potassium dichromate	81	61		
Nickel sulphate	64	90		
Formaldehyde	40	77		
p-Phenylenediamine	26	68		
Balsam of Peru	56	59		
Neomycin sulphate	93	89		

ferences in the incidence of positive reactions found at the various hospitals. Dermatitis of the hands was more frequent among males than among females.

The age distribution varied greatly (Fig. 2). Patients over 70 did not appear in the Stockholm material but were very common in Gothenburg. The age distribution showed no particular trend in men. In Bergen, Copenhagen and Lund few women between 25 and 45 were referred to the contact clinic.

Table 4. Correlations of history, examination and patch test results in 609 females

Domestic work only Atopic dermatitis		caliz Caliz	Lower leg		Dichromate	N _{Ickel}	Formaldehyde		Balsam of Peru	Neomycin	Dichromate	N _{Ic} kel	Formaldchyde	рРД	Balsam of Peru	Neomycin	Routine series	Not routine series	Multiple sensitivity		
233 21	-	16	40	91	-	25	10	19		12	,	1		8	22	12	84	29	69		Domestic work only
			_		5				33	13	3	23	9		-						
63	1	7	2	24	0	1	2	3	9	0	0	1	0	0	3	0	10	3	9	_	Atopic dermatitis
	346	33	14	88	12	31	16	26	37	7	8	28	10	14	14	7	111	41	89	Localization	Hand
	L	54	8	12	2	4	2	7	2	1	2	3	2	4	I	1	22	9	15	aliz	Foot
			86	12	1	7	4	7	26	17	0	7	3	6	23	16	40	12	40	atio	Lower leg
				267	5	28	16	17	21	7	5	26	16	10	13	5	74	33	1 2	ň	Other sites
					18	2	2	2	0	0	01	2	I	2	0	0	5	3	6		Dichromate
						52	4	3	3	4	3	47	4	2	2	4	27	6	32	2	Nickel
							30	3	4	1	2	3	23	2	3	1	8	5	14	eac	Formaldehyde
								37	12	4	2	2	2	25	6	3	23	9	30	Reactions	PPD
								Į	73	14	0	3	3	9	42	13	43	11	50	S	Balsam of Peru
									j	27	0	4	0	4	12	24	14	4	23		Neomycin
											1	3	1	2	0	0	6	2	7		Dichromate
												47	3	2	2	4	26	5	31		Nickel
											,		23	1	2	0	7	4	10	Relevance	Formaldehyde
												-		25	5	3	12	7	18	van	PPD
													,		43	11	27	7	33	ce	Balsam of Peru
																24	13	3	21		Neomycin
																	184	40	128	R	Routine series
																		75	49	act	Not routine series
																			152	Reactions	Multiple sensitivity

The relevance of test reactions differs considerably between the substances and with the same substance between the sexes [Table 3].

The Correlation Tables 4 and 5 summarize the results of the whole study.

Contact Sensitivities in Domestic Workers

The most frequent sensitivities found among those doing solely housework were balsam of Peru (14%), nickel (10%) and PPD (8%). These percentages among all fe-

males were 12 %, 8 % and 6 %, respectively.

Although sensitivity to chromium has previously been associated with housework (1,7), chromium sensitivity was rare (2%) among those in housework only as well as in the total female material (3%).

Atopic Dermatitis—Contact Sensitivity

Some authors state that false positive reactions to metals are common in patients with atopic dermatitis. In the present material,

Table 5. Correlations of history, examination and patch test results in 418 males

Domestic work only Atopic dermatitis	Hand	Foot	Lower leg	Other sites	Dichromate	Nickel	Formaldehyde	PPD	Balsam of Peru	Neomycin	Dichromate	Nickel	Formaldehyde	PPD	Balsam of Peru	Neomycin	Routine series	Not routine series	Multiple sensitivity		
	L	ocali	izati	on			Reac	tion	S			1	Rele	vanc	e		Re	acti	ons		
710	3	0	2	5	0	0	0	0	0	0	0	0	0	0	0	0	3	0	I		Domestic work only
35	T 22	1	7	15	2	I	4	2	0	I	1	0	I	I	0	1	3	I	2		Atopic dermatitis
_	288	60	41	83	34	8	17	17	32	7	28	5	6	4	17	7	82	36	68	Lo	Hand
		80	27	16	12	4	3	10	7	3	8	2	I	3	4	3	22	9	19	cali	Foot
			18	38	10	2	5	4	9	5	5	I	2	2	5	5	27	7	21	Localization	Lower leg
				178	14	6	7	9	15	10	10	3	1	2	11	9	47	21	42	ň	
					41	6	3	3	2	I	33	5	I	0	1	I	17	3	25		Dichromate
						14	1	2	1	1	4	9	0	0	1	I	3	0	8	R	Nickel
							20	2	2	I	2	0	8	t	I	I	11	2	1 [Reactions	Formaldehyde
								23	4	2	2	I	Ī	6	3	2	11	5	15	ion	PPD
									39	2	2	1	1	1	22	2	15	9	20	0.	Balsam of Peru
									Į	15	0	0	0	0	2	14	9	2	II		Neomycin
											33	4	1	0	I	0	13	2	20		Dichromate
												9	0	0	I	0	2	0	6	R	Nickel
													8	1	1	0	3	I	4	elev	Formaldehyde
														6	1	0	4	2	5	Relevance	PPD
														Ų	22	2	11	6	14	е	Balsam of Peru
																14	8	2	10		Neomycin
																Ų	107	17	71	Rea	Routine series
																	į	50	26	Reactions	Not routine series
																			91	Suc	Multiple sensitivity

Table 6. Incidence of positive reactions to substances other than the six included in the study and incidence of sensitivity to several substances not chemically related

(i.e. multiple sensitivities)

	418	males	609 females				
	Mean (%)	Range (%)	Mean (%)	Range (%)			
Substances in routine test series	27	8-39	29	10-35			
Substances not in the routine test series	13	7-18	13	9-18			
Multiple sensitivities	22	14-34	25	14-32			

however, reactions to nickel and chromate were uncommon both in men and women with past or present atopic dermatitis. Among the 63 atopic females, one had a relevant positive reaction to nickel. Chromate sensitivity was found in none of 63 women, and in two of 35 men. In only one of the two cases could clinical relevance be found. In view of the repeated discussions of the frequency of sensitivity to neomycin among atopics, it is noteworthy that none of the 63 females and only one of the 35 males had positive reactions to it.

Correlations of Reactions to Certain Test Substance to Site of Dermatitis

Sensitivity to balsam of Peru was the most frequent sensitivity in eczema of the legs, both relatively and absolutely among women, but relatively only among men. Sensitivity to the other topical remedy, neomycin, was also seen most often in cases with leg eczema. PPD sensitivity was most often seen in cases of foot eczema, being the most frequent allergen in female cases with eczema in the feet, and exceeded only by dichromate sensitivity among men.

Relevance of Test Reactions

The proportion of test reactions considered to be relevant varied considerably, because its evaluation is subjective and based on an agreement between the patient and the examiner. The relevance of nickel sensitivity varies, depending on the importance paid to manual nickel contact by the examiner. In women, nickel reactions were considered to be relevant in a high proportion of cases. Formaldehyde sensitivity was rarely found

to be relevant in males, but commonly in females. PPD sensitivity was relevant in 26 per cent of men and 67 per cent of females. The relevance was frequently found only in female cases with leg eczema. Sensitivity to balsam of Peru may often be considered relevant if taken to comprise all perfumes but rarely if these are excluded.

Multiple Sensitivities

Multiple sensitivities were found on an average in 22 per cent of men and 25 per cent of women (Tables 4, 5, 6, Fig. 3). It was at about the same level in cases with localization other than legs. In leg eczema multiple sensitivity was found in 46 % of females and in 26 % of the males.

Comments

In previous papers we have shown that, e.g. the sex distribution of the patients tested is decisive for the results of standard patch testing (4, 5). Consequently, it is impossible to compare incidence of sensitivities based on total figures collected at a hospital unless a number of factors are taken into account. The range of differences in the age and sex of the patients seen and of the localization of dermatitis appears from the present study. It was realized in advance that the number of the patients included in the study would be too small to permit definite conclusions as to the influence of the factors mentioned on the type of sensitivities prevalent in the area. Still certain conclusions may be drawn.

The percentage of patients with different localizations of eczema varies greatly from one hospital to another. Sensitivity to local

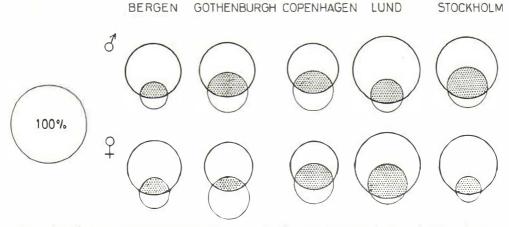


Fig. 3. Incidence and coincidence (hatched area) of hand dermatitis (upper circle) and multiple sensitivities (lower circle). The area represents the parcentage of the total number of patients tested in each sex.

therapeutics is particularly common in eczema of the legs. Thus the incidence of sensitivity to balsam of Peru and to neomycin in a particular hospital must to a large extent be decided by the number of patients with leg eczema tested. The same factor tends to increase the incidence of multiple sensitivities, and indicates that the high incidence observed in Gothenburg among cases with eczema other than on the hands (Fig. 3) may be due to extensive testing of women with eczema of the leg at that particular clinic.

Neomycin elsewhere reported to be a common allergen in atopics was significantly lower in atopics than in other patients. Only one of the 98 atopic patients had a positive reaction to neomycin.

SUMMARY

In an earlier study at six Nordic contact allergy clinics regional differences in the frequency of positive skin reactions to certain substances were noted. They could partly be explained by differences in the categories of the patients tested at the various clinics. The aim of the present study was to illustrate the influence of certain factors, such as sex, age and type and localization of eczema upon the results of patch tests.

The material comprised 1027 consecutive

patients seen during the same period of time at the five clinics participating in the study. Results with potassium dichromate, nickel sulphate, formaldehyde, p-phenylenediamine, balsam of Peru and neomycin sulphate were primarily analyzed, but reactions to a larger standard test series, clinical relevance of the reactions and occurrence of multiple sensitivities were also taken into consideration. The results illustrate the differences in the patient materials in various clinics and indicate that the frequencies of positive reactions to various substances and of occurrence of multiple sensitivities are greatly influenced by the selection of patients, especially by the sex distribution and the localization of eczema.

REFERENCES

- Forck, G.: Zunahme von Metallallergien bei Hausfrauen, XIII. Congressus Dermatologiae, Vol. 1, p. 270. Springer-Verlag, Berlin 1968.
- Magnusson, B., Blohm, S. G., Fregert, S., Hjorth, N., Høvding, G., Pirilä, V. and Skog, E.: Standardization of routine patch testing I. Proc. Northern Dermat. Soc., p. 126, 1962.
- 3. Magnusson, B., Blohm, S. G., Fregert, S., Hjorth, N., Høvding, G., Pirilä, V. and Skog, E.: Routine patch testing Il.—Proposed basic series of test substances for Scandinavian countries and general remarks

- on testing technique. Acta derm.-venereol. 46: 153, 1966.
- Magnusson, B., Blohm, S. G., Fregert, S., Hjorth, N., Høvding, G., Pirilä, V. and Skog, E.: Routine patch testing III.—Frequency of contact allergy at six Standinavian clinics. Acta derm.-venereol. 46: 396, 1966.
- Magnusson, B., Blohm, S. G., Fregert, S., Hjorth, N., Høvding, G., Pirilä, V. and Skog, E.: Routine patch testing IV.—Sup-
- plementary series of test substances for Scandinavian countries. *Acta derm.-venereol.* 48: 110, 1963.
- 6. Magnusson, B. and Hersle, K.: Patch test methods. I. A comparative study of six different types of patch tests. *Acta derm.*venercol. 45: 123, 1965.
- Skog, E. and Thyresson, N.: The occupational significance of some common contact allergens. Acta derm.-venereol. 33: 65, 1953.