SKIN REACTIONS TO OINTMENT BASES*

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Before attending a dermatological clinic nearly all patients have been treated with cosmetic or pharmaceutical creams or ointments. Whatever the active ingredients, the bases are formulated very much according to principles everywhere, and a number of the creams used are manufactured by international firms. Experience of reactions to such ointment bases collected in one country may, therefore, have a general application.

Ointments consist of fats of mineral or vegetable origin, such as vaseline, liquid paraffin and olive oil. Emulsifiers and water may be added to form emulsion creams. Common emulsifiers used are lanolin and its derivatives, whether esters or higher alcohols. Emulsion creams are excellent media for the proliferation of moulds, so that preservatives need to be added.

TABLE I

RESULTS OF ROUTINE PATCH TESTS 1962.
1,664 CONSECUTIVE PATIENTS WITH ECZEMA.

Coal tar	72	(4.3%)	Nickel	79	(4.7%)
Wood tars	66	(4.0%)	Primula	60	(3.5%)
Balsams	54	(3.2%)	"Rubber"	59	(3.5%)
Neomycin	51	(3.0%)	Formaldehyde	45	(2.7%)
Balsam of Peru	40	(2.4%)	Dichromate	44	(2.6%)

Lanolin and derivatives ... ... 38 cases (2.28%)
Wool alcohols (Ph. Dan.) ... ... 27 cases (1.62%)

The results of a routine series of patch tests performed on 1664 consecutive patients with eczema at the Finsen Institute during 1962 are shown in Table I to illustrate the magnitude of the problem. Nearly half of all positive patch tests are due to therapeutic agents of some kind. Sensitivity to lanolin and its derivatives, is about as common among our patients as sensitivity to dichromate or formaldehyde.

PRESERVATIVES

A number of the preserving agents used are occasional contact sensitizers. My own interests in the subject stems from a study of paraben esters, which are the preservatives mainly used in Denmark (Hjorth, 1961).

Paraben Esters

The most commonly used preservatives are methyl and propyl para-hydroxybenzoates (parabens Fig. 1), usually added to creams in concentrations between 0.1 and 0.3%. The methyl ester is to some extent soluble in water, the propyl ester is nearly insoluble in water but soluble in liquids.

Owing to its fungicidal properties, ethyl paraben has been widely used in Denmark for tinea pedis since1938. Therapeutic dermatitis from it was first reported in 1940, and since then more than 140 cases have been diagnosed as such at the Finsen Institute.

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*Adapted from a paper presented at the Consultants' Seminar on 19th April, 1963.

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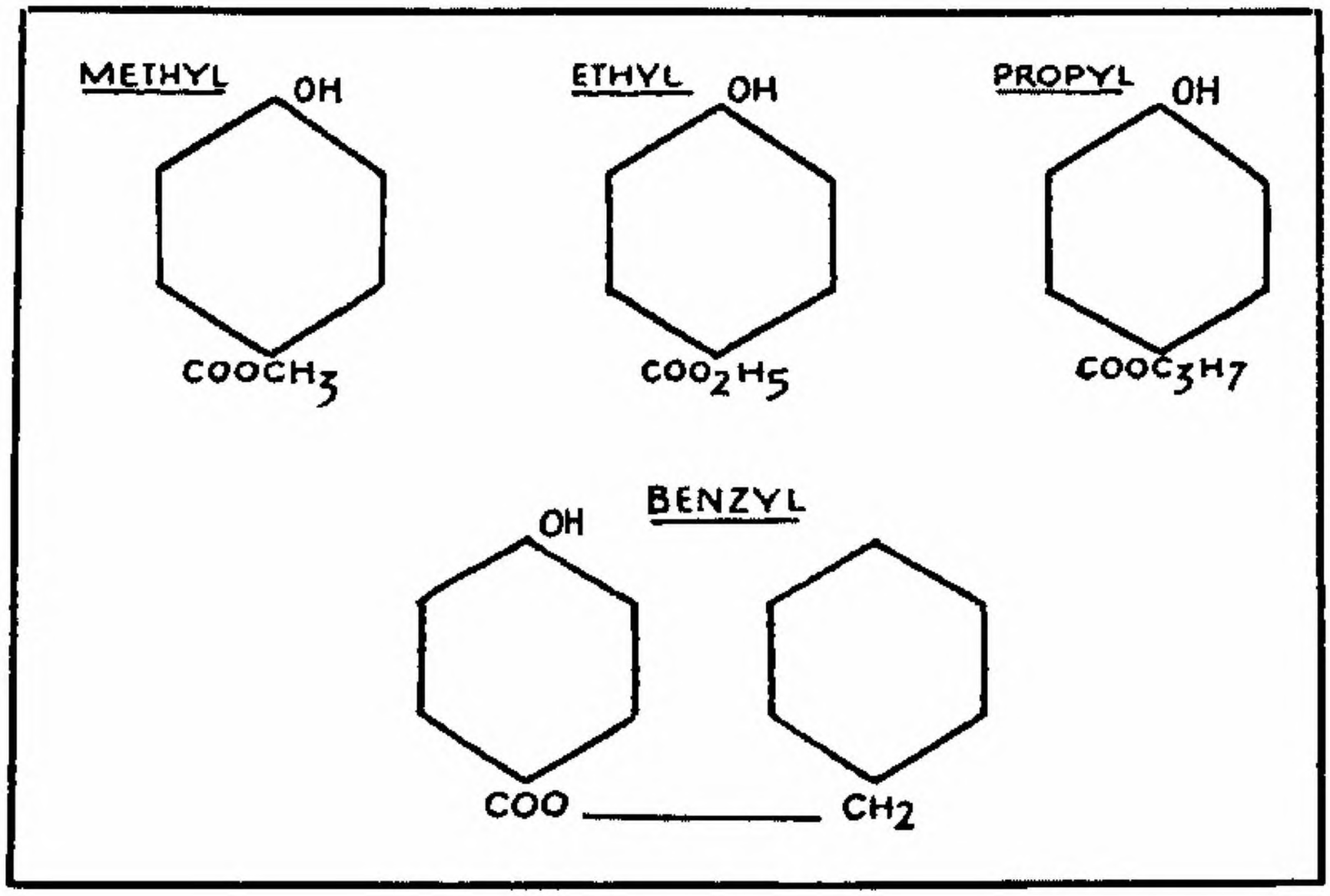

FIGURE I
p-OXYBENZOIC ACID ESTERS (PARABEN-ESTERS)

TABLE II
PATCH TESTS WITH PARABENS

	Total	*Positive*	*Negative*
Selected patients			
1947	4	1	3
1950	42	8	34
1953	100	10	90
Consecutive patients			
1954–55	2170	25 (1.15%)	2145
1959–61	3629	(41 1.13%)	2588

About one in a hundred patients with eczema are sensitive to paraben-esters, the incidence in 1954–1955 being 1.15 per cent, and in 1959–1961 being 1.13 per cent, as shown in Table II. In previous years only a selected number of patients were tested, but as may be seen, the more patients tested, the larger is the number of cases discovered.

The topical preparations used in Denmark all have a very high content of paraben-ester, for example, Amycen of the Danish pharmacopoeia.

Amycen Ph. Dan. —Mycocten		
Ointment	Ethyl paraben	5%
	Salicylic acid	3%
Solution	Ethyl paraben	5%
	Salicylic acid	2%
Powder	Ethyl paraben	5%
	Salicylic acid	5%

When aureomycin ointments were introduced with a similar excessive concentration, single cases were observed in Germany (Schultheiss, 1958) and in England (Sarkany, 1960).

Aureomycin		
Ointment	Methyl paraben	2.4%
	Propyl paraben	0.6%
	Aureomycin	3%
Powder	Methyl paraben	20%
	Aureomycin	20%
Syrup : in 5 ml.	Methyl paraben	4 mg.
	Propyl paraben	1 mg.
Achromycin Ointment :	No parabens	
Achromycin Ointment with hydrocortisone : as Aureomycin ointment.		

In a preliminary study in 1954, eight out of nine patients sensitive to the Danish Mycocten ointment were found also to show a positive reaction to aureomycin ointment, which indicated that cross-sensitivity between the various esters was very common. This is also apparent from our later studies, which show that about two-thirds of the patients sensitive to one of the paraben-esters will also react to one or several other esters (Table III). The sensitivity, however, rarely extends to other aromatic substances, as appeared from a study of fourteen patients tested with a multitude of these.

TABLE III

CROSS SENSITIVITY BETWEEN PARABEN ESTERS. 32 CASES TESTED WITH 5 PER CENT PARABEN ESTERS IN PETROLATUM OR IN EUCERIN AND WATER EQUAL PARTS

Note.—One case was not tested with propyl paraben or benzyl paraben.

			Methyl Paraben		Ethyl Paraben		Propyl Paraben	
			pos.	neg.	pos.	neg.	pos.	neg.
		No. of cases	21	11	27	5	22	9
Ethyl Paraben	pos.	27	18	9				
	neg.	5	3	2				
Propyl Paraben	pos.	22	15	7	20	2		
	neg.	9	5	4	7	2		
Benzyl Paraben	pos.	14	10	4	12	2	13	1
	neg.	17	16	7	15	2	9	8

Nineteen patients who reacted to an ointment containing a mixture of paraben-esters totalling 14%, were tested with four esters, each in four concentrations, varying from 5.0% down to 0.1%. All patients reacted to one or several of the 5.0% ointments, 13 to 1%, 11 to 0.5%, and 5 to 0.1%. The degree of sensitivity to the various esters may differ in patients sensitive to several ; but patients presumably sensitized by ethyl parabens may sometimes show a higher degree of sensitivity to one of the other esters.

It appears from the table that patch tests should be performed using a concentration of not less than 5% of paraben.

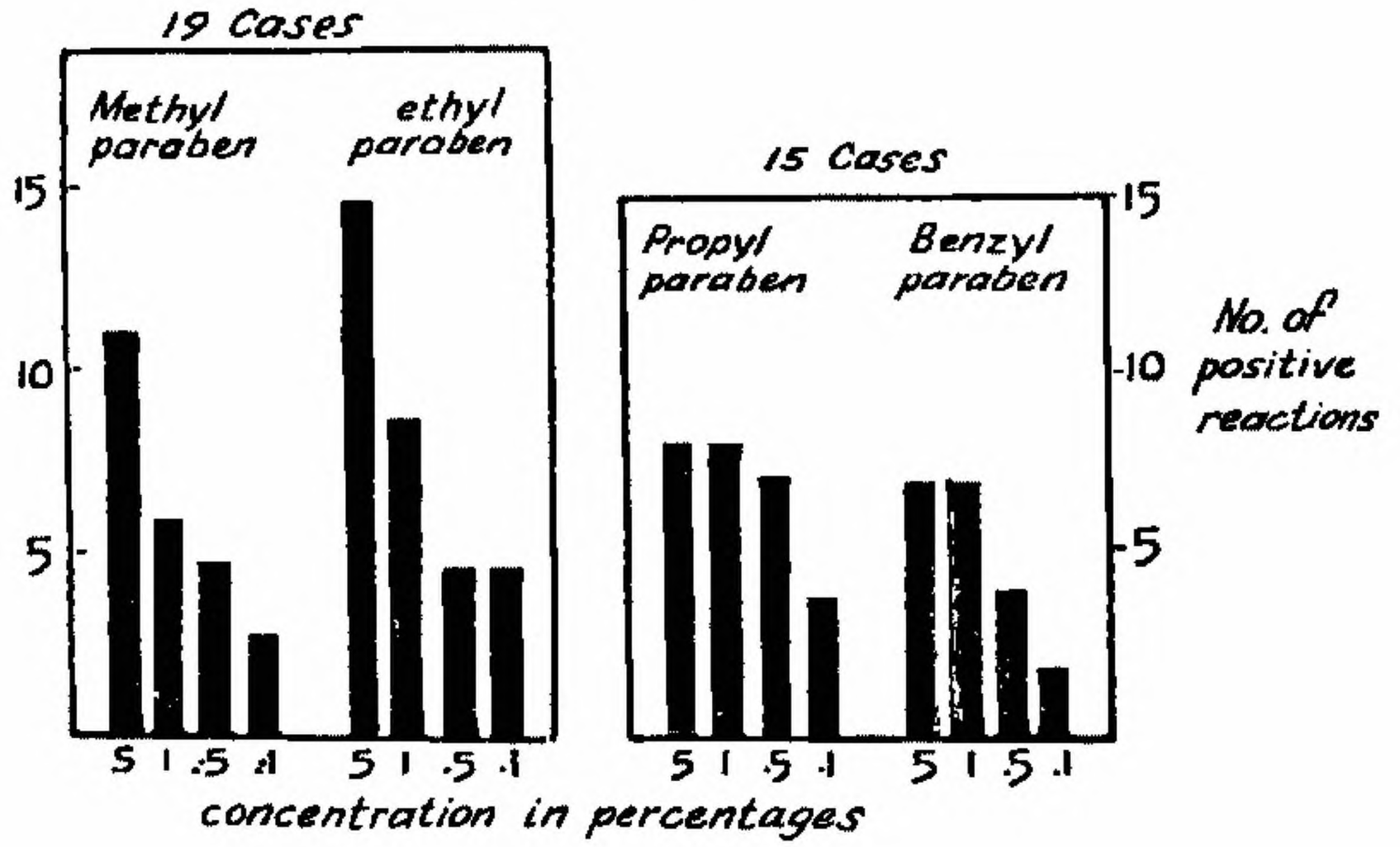

Table IV
Level of Sensitivity to Paraben Esters
Results of simultaneous patch tests with four different concentrations of paraben esters on 15 cases. Four additional cases were tested only with the methyl and ethyl esters.

The degree of sensitivity determined by patch tests is not an infallible guide to the clinical tolerance to creams containing paraben-esters. Flare up of an eczema may occur after treatment with cream, even in patients with a patch test threshold of 5%. Positive reactions to different hydrocortisone creams were obtained in seven out of ten patients tested. Treatment with a hydrocortisone cream containing parabens may in such cases lead to a very protracted course of eczema, without improvements and without a local reaction indicating therapeutic sensitivty.

The patients included in the study have nearly all been sensitized by the therapeutic use of paraben-esters in high concentrations. Otherwise females would probably have dominated in the total.

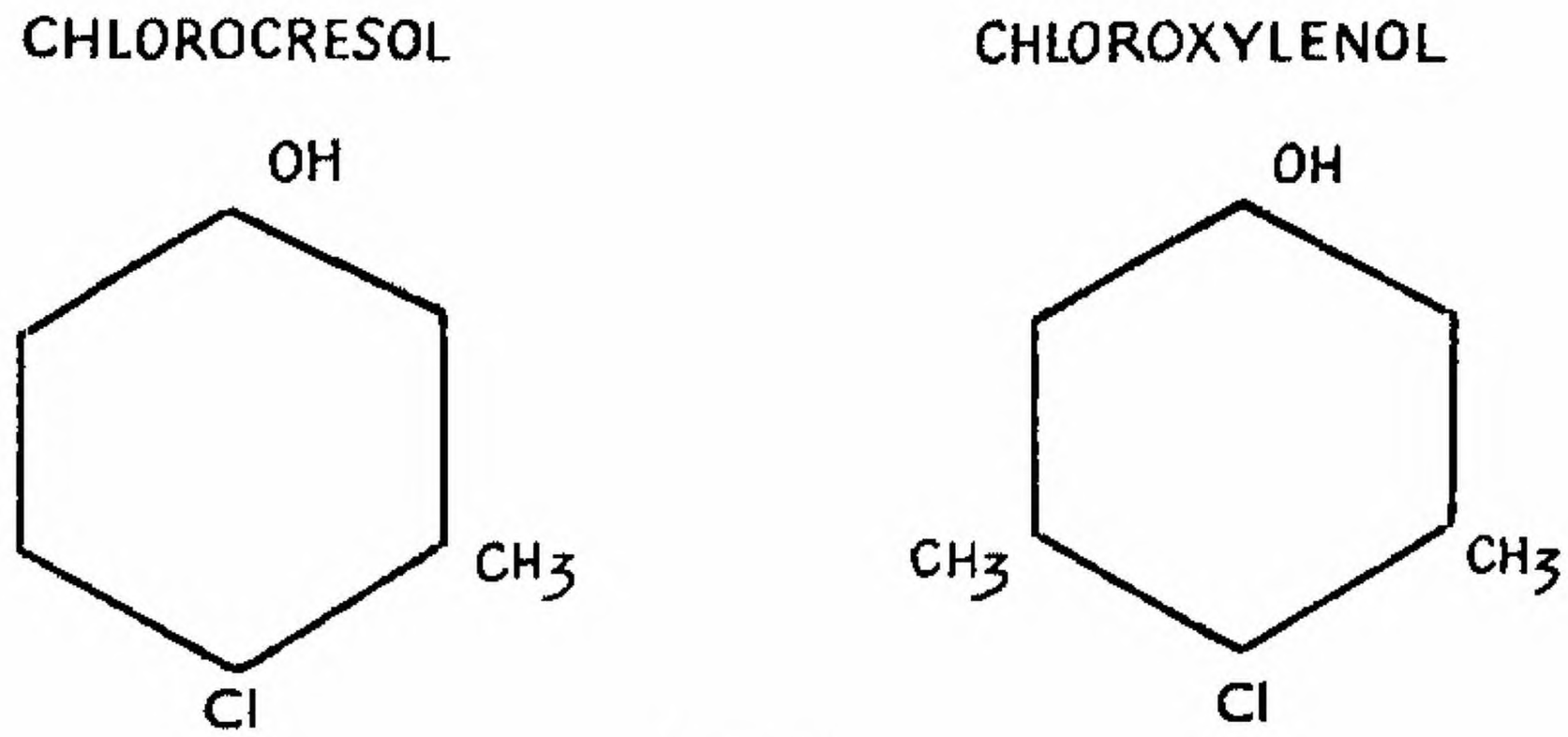

Figure 2
Structural Formulae of Chlorocresol and Chloroxylenol

Chlorocresol

Chlorocresol is much favoured as a preservative by the British National Formulary and is used in hydrocortisone creams, barrier creams and so on. It is little used in Denmark. The close relationship to chloroxylenol (Fig. 2), highest but one on the list of causes of dermatitis medicamentosa in England (Calnan, 1962), might merit attention. Cross-sensitization does occur, as we have been able to verify in three patients, and the problems posed by this in Great Britain must be as important as the one posed by sensitivity to paraben-esters in Denmark.

Sorbic Acid

Sorbic acid (CH.CH : CH.CH : CH.COOH) has some application as a preservative. It has recently been studied by Trolle-Lassen and Hjorth (1961). In spite of the fact that it has not yet been used in Denmark, five (0.3%) of 1,489 patients with eczema tested with it were found to be sensitive. The suitable concentration for testing is 2% or 5% in soft paraffin. The patients were probably sensitized from natural sources such as plants or berries. Apart from showing that it might act as a sensitizer, the study referred to above also indicated that it is more irritant than the paraben-esters. We further found that sorbic acid provoked an immediate reaction when applied as patch tests, appearing after ten minutes and persisting up to thirty minutes after application. The immediate response may be ascribed to the acid reaction since it was also found in patch tests with benzoic acid, a finding of interest in relation to patch tests with Whitfield's ointment.

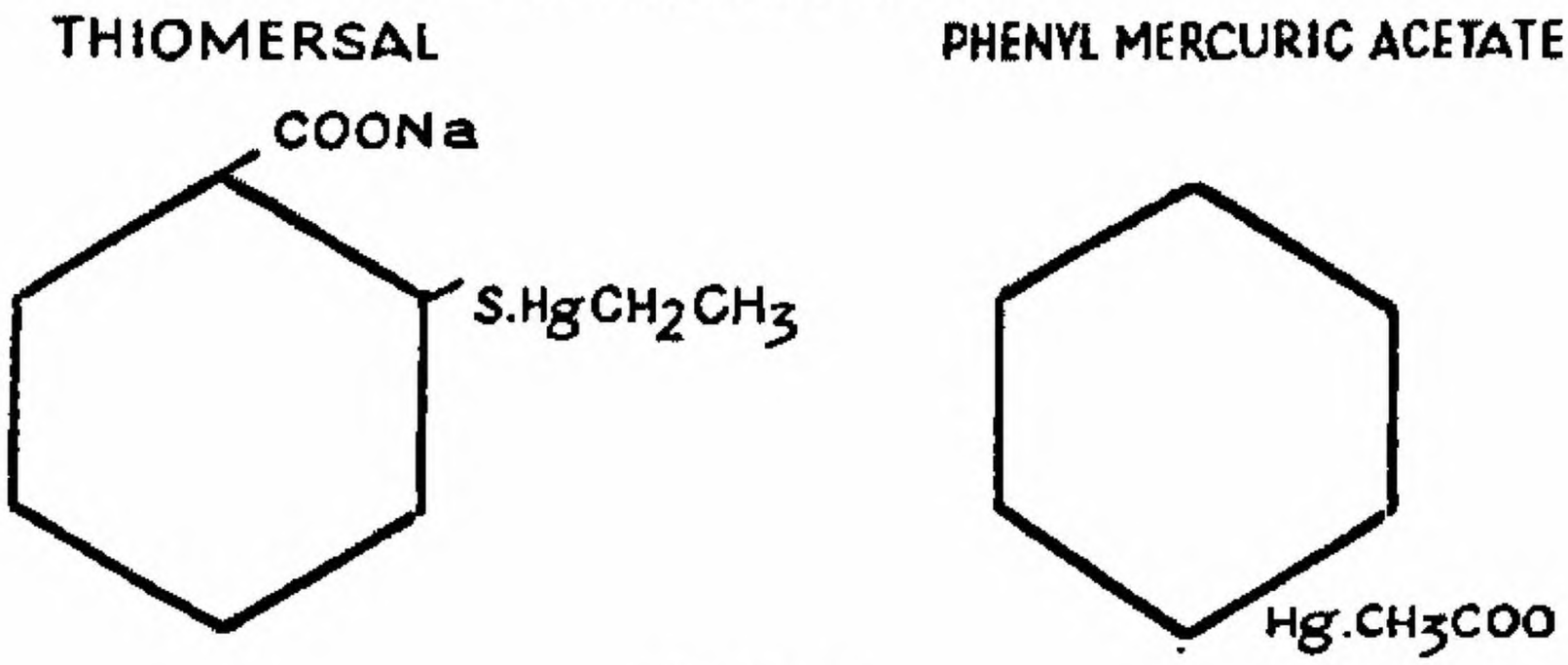

FIGURE 3
STRUCTURAL FORMULAE OF THIOMERSAL AND PHENYL MERCURIC ACETATE

Organic Mercury Compounds

Organic mercury compounds such as phenyl-mercuric-acetate and thiomersal (Fig. 3) are used in some creams and eyedrops. It may be of interest that the mercury ion does not cross-sensitize to the organic compounds. Patch tests with 0.1% phenyl-mercuric-acetate invariably provoke a primary irritant reaction, both in patients sensitive to mercury and in controls. Patch tests with 0.1% performed on thirty three patients sensitive to mercury (0.1% mercuric chloride) invariable gave negative results (Svendsen, 1961). Likewise, Calnan (1962) found only three patients sensitive to thiomersal, in spite of frequent positive reactions to mercuric chloride.

In conclusion, it may be said that the preservatives used in ointments rarely give rise to primary sensitization owing to the low concentrations employed. Most preservatives, however, are used for other purposes as well, so that primary sensitization may derive from these other sources. A patient sensitive to a preservative in creams is destined to go from one attack of dermatitis to another, because a cream will almost always be the first resort either of the patient or his general practitioner, so that a trifling skin complaint may develop into a persistent eczema.

Base Constituents

Lanette Wax or Emulsifying Wax

Because of the frequency of sensitivity to lanolin and paraben-esters, we have made an extensive study of a number of other types of ointment constituents, especially those used as emulsifiers. The method used for the study was to employ different vehicles for each of the substances included in our routine patch test series.

Lanette wax SX and emulsifying wax are very useful emulsifiers for creams of the oil-in-water type. They consist chiefly of cetyl and stearyl alcohol, with 10 per cent of sulphated esters of fatty alcohlos. A sulphonamide cream (Lucosilsalve* 2.5%) containing lanette wax has been included in our standard patch test series for many years, although positive reactions have not always been analysed. Table V shows the results for the years 1943, 1959 and 1962. Lanette wax has been the major cause of reactions to the sulphonomide cream, and is nowadays the only cause of reaction to it. The table also demonstrates one of the most important causes of overlooking sensitivity to any type of constituent to a cream base, namely, that a positive patch test to a cream may be wrongly ascribed to one of the active ingredients which is known to be a sensitizer.

Table V
Causes of Sensitivity to a Sulphonamide Cream, Lucosilsalve 2.5%
Cream : Vaseline, Lanette wax, water and paraben esters 0.2%.
Sulphonamide : Sulphamethylthiodiazol 4% aq.

Year ...	1943	1959	1962
Lucosilsalve, total positives ...	17	11	25
Analysis :			
Sulphonamide and cream positive	6	1	0
Sulphonamide pos. cream neg. ...	3	0	0
Cream pos. sulphonamide neg. ...	8	7	13
Both negative	?	3	12
Sulphonamide total positives ...	9	1	0
Cream total positives	14	10	13

Lanette waxes are used in a great number of pharmaceutical creams. Concommittent sensitivity to lanette wax and to lanolin is infrequent ; in fact, it only occurred in six out of fifty patients sensitive to lanolin, little more than might be explained by mere coincidence.

Table VI
Results of Patch Tests with Aliphatic Alcohols
(1,664 Consecutive Patients)

Substance	*Conc.*	*Vehicle*	*Cases positive*
C_8 Octyl alcohol ...	5%	vas.	11
C_{10} Decyl alcohol ...	5%	vas./ol. oliv.	15
	10%	vas.	22
C_{12} Lauryl alcohol ...	5%	vas.	4
	10%	vas.	15
C_{14} Myristyl alcohol ...	5%	vas.	0
	10%	vas.	21
C_{16} Cetyl alcohol ...	30%	vas.	2
C_{18} Stearyl alcohol ...	30%	liq. paraff.	4
2-Octyl dodecanol ...	30%	vas.	6
Oleyl alcohol ...	30%	vas.	10
C_{34} Cetostearyl alcohol...	30%	liq. paraff.	8

*Sulphamethylthiodiazole.

Aliphatic Alchohols

The alcohols with 8, 10, 12 and 14 carbon atom chains are mainly used in the manufacture of detergents, while those with 16 and 18 carbon chains are used for creams. The lowered numbered series are primary irritants, but frequently the reactions provoked are indistinguishable from true eczematous reactions. I have included these alcohols in Table VI just to indicate the maximum permissible concentration for patch testing with them. It can be seen that the number of patients with sensitivity is not inconsiderable. Positive reactions to the higher alcohols were very rare.

It will be noted that there is some inconsistency in the results since reactions to alcohol C_{30} are more frequent than to each of C_{16} and C_{18}, although C_{36} is supposed to be a mixture of the latter. Among the straight chain alcohols, the unsaturated oleyl alcohol appears to be quite a frequent sensitizer, as previously shown by Calnan and Sarkany (1960).

TABLE VII
REACTIONS IN TEN PATIENTS SENSITIVE TO OLEYL ALCOHOL

Case No.	1	2	3	4	5	6	7	8	9	10
Oleyl alc	++	(+)	++	++	++	+++	+++	+++	++	++
Decyl alc	+	nze.	neg.	neg.	neg.	neg.	neg.	neg.	neg.	neg.
Myristyl alc	neg.	++	neg.	neg.	neg.	neg.	neg.	neg.	neg.	neg.
Stearyl alc	+	neg.	neg.	++	+	neg.	neg.	neg.	neg.	neg.
Cetostearyl alc	neg.	neg.	++	neg.	neg.	neg.	neg.	neg.	neg.	neg.
Lanette wax	neg.	neg.	neg.	++	0	+++	++	+	neg.	neg.
Lanette wax cream ...	neg.	neg.	neg.	++	++	++++	+++	neg.	neg.	neg.
Lanolin	neg.	neg.	neg.	neg.	neg.	neg.	neg.	neg.	±	neg.
Lanolin alcohols ...	neg.	neg.	neg.	neg.	neg.	neg.	neg.	neg.	++	neg.

A wide variation in the patterns of sensitivity is noticeable (Table VII). The alcohols used for the experiments were of a high grade commercial quality, but this only indicates a minimum content of 95% or 97% of the substance indicated on the label. Positive reactions may, therefore, be due to impurities but Table VII indicates that patients are not of necessity sensitive to identical impurities.

TABLE VIII
REACTIONS IN PATIENTS SENSITIVE TO STEARYL ALCOHOL

Case No.	77534	78769	80074	80030
Stearyl alcohol	+	+	++	+++
Oleyl alcohol	++	++	++	neg.
Lanolin alcohols	neg.	neg.	neg.	++
Lanette wax cream	++	neg.	++	neg.

Stearyl alcohol gave reactions in four patients only, three of which were sensitive to oleyl alcohol (TableVIII). The stearyl alcohol used had a minimum purity of 97% and, if the positive reactions had been due to a content of oleyl alcohol, these three patients should have been sensitive to less than 1% oleyl alcohol in vaseline, which is not very likely. Presumably there must have been a cross-sensitization between the two, the saturated and unsaturated alcohols of identical chain length.

TABLE IX
PATCH TEST REACTIONS TO GLYCERYL MONOSTEARATE AND MONOLEATE

Substance	*Conc.*	*Vehicle*	*No. of cases with pos. reactions*
Glyceryl monoleate ...	30%	liq. paraff.	2 cases
Glyceryl monostearate ...	30%	vaselin	1 case
Isopropyl myristate ...	30%	vaselin	No cases

A single case of sensitivity to glyceryl monostearate was recently published (Schwartzberg, 1961) but our study has shown that sensitivity to it is of no practical importance. The same applied to glyceryl monoleate and isopropylmyristate, which are also widely employed in creams.

Throughout this study we have encountered difficulties when trying to analyse sensitivities to ointments. Very often analysis with each of the ingredients results in a negative reaction to all. Positive results might have been obtained by increasing the concentrations of each of the ingredients, but there are two pitfalls in this respect ; firstly, the primary irritant properties of the alcohol ; and secondly, the technical problem of getting a suitably concentrated solution.

TABLE X
REPORTED INCIDENCE OF SENSITIVITY TO LANOLIN AND EUCERIN

Author	*Selection of patients*	*Substance tested*	*No. examined*	*Positive*
Warshaw (1953), New York	Contact Dermatitis	Lanolin	1430	15 (1.0%)
Baer et al. (1955), New York	Dermatitis medicament	Lanolin	637	28 (4.4%)
	,,	Oxycholesterol-petrolatum oint.	100	11 (11%)
Bandmann (1957), Munich	Contact Dermatitis	Eucerin	4000	10(0.25%)
Finsen Institute (1961) (1962)	Eczema	Eucerin	1878	31 (1.8%)
	,,	Wool Alcohols	1664	27 (1.6%)

Lanolin and its Derivatives

Sensitivity to lanolin has in the past been considered quite a rarity, but it appears to be among the most important causes of dermatitis medicamentosa (Warshaw, 1953 ; Baer et al. 1955 ; Bandmann, 1957). The incidence at the Finsen Institute is about 1.8% (TableX). Sensitivity to it is often overlooked, as mentioned by Calnan (1962).

The nature of the allergenic susbstance has been studied by Sulzberger and collaborators (1950, 1953), and later by Everall and Truter (1954). In a study of twenty-two lanolin hypersensitive patients Sulzberger and Warshaw found positive reaction to the alcohol fractions. Although the patients showed some variation in their pattern of sensitivity, the authors presumed that the aliphatic alcohols were the major allergens. Everall and Truter's study was performed on one patient, tested with a number of fractions obtained by chromatographic separation. They were able to isolate two distinct allergens, of which one was chemically identified. Their patient did not show any reaction to the aliphatic alcohols. Presumably, just like patients sensitive to Balsam of Peru, few of the patients sensitive to lanolin have identical patterns of sensitivity. This can only be determined by an extensive study on the principles shown by Everall and Truter.

Both groups of workers agreed that the allergens were found in the alcohol fraction. Curiously enough, a number of purified lanolins are based exclusively on these and and may therefore be presumed to give more frequent reactions than lanolin itself. Such concentrates of alcohols or wool alcohols are included in the British and Danish Pharmacopoeias and much used in the National Formularies. Eucerin is another concentrate and contains 6% purified lanolin alcohols in vaseline. The oxycholesterol petrolatum ointment mentioned by Baer et al. (1955) is an imitation of eucerin.

In the series of routine patch tests proposed by Bonnevie in 1939, lanolin was used as a vehicle for several substances such as salicylic acid and Balsam of Peru. For many years, however, it was not realised that positive reactions to salicylic acid in lanolin were most often due to the latter, because separate tests with lanolin and with salcylic acid usually gave negative reactions in patients sensitive to the mixture. Simultaneous positive reactions to salicylic acid and Balsam of Peru, may suggest the presence of lanolin sensitivity, in spite of the possible negative reactions with the separate substances. That such patients were sensitive to lanolin remained as postulate until lanolin alcohols were introduced into the patch tests series.

TABLE XI
COMPARISON OF REACTIONS TO VARIOUS TYPES OF LANOLIN

Lanolin with salicylic acid 5%	*Lanolin*	*Eucerin (Eucerit 6% in vas.)*	*No. of patients*
+	+	+	10
+	neg.	+	15
+	neg.	neg.	3
neg.	neg.	+	12
Total positive : 28	10	37	40

As appears from Table XI, reactions to eucerin are far more frequent than reactions to either lanolin or salicylic acid in lanolin. On the other hand, there is good agreement between reactions to salicylic acid in lanolin and eucerin, since two of the three patients reacting only to salicylic acid in lanolin, were sensitive to some derivative of eucerin. Thus, salicylic acid promotes the penetration of allergens into the skin so that a low level of sensitivity to lanolin will be detected (Table XI). Another way of detecting a low degree of sensitivity is to use some patch tests with wool alcohol, which we have used at a concentration of 30% in a mixture of olive oil and vaseline. Among twenty-eight patients with positive reactions to wool alcohol, twenty had positive reactions to either eucerin or lanolin. Non-specific reactions to salicylic acid in lanolin do occur but they are not very frequent. Among forty con-

TABLE XII
RESULTS OF ROUTINE PATCH TESTS IN 13 PATIENTS SENSITIVE TO LANOLIN

	Anhydr. woolfat	*Sali-Cylic acid*	*Balsam of Peru*	*P.P.D.*	*P-amino phenol*	*Pyro-gallol*
Conc.	*Pure*	*5% in lan.*	*25% in lan.*	*2% in lan.*	*2% in lan.*	*5% in lan.*
Case 1	+ + +	+ +	+	neg.	neg.	neg.
2	+ + +	+ + +	neg.	neg.	neg.	neg.
3	+ + +	+ +	+ +	neg.	neg.	neg.
4	+ + +	+ + +	+	neg.	neg.	neg.
5	+ +	+ +	neg.	neg.	neg.	neg.
6	+ +	+ +	+ +	neg.	neg.	neg.
7	+ +	+ +	neg.	neg.	+ +	neg.
8	+ +	+ +	neg.	neg.	neg.	neg.
9	+ +	+ +	+ +	neg.	(+)	neg.
10	+ +	+ + +	+ + +	neg.	neg.	neg.
11	+ +	+ +	neg.	neg.	neg.	neg.
12	+ +	+ + +	+ + +	neg.	+ +	neg.
13	+	+ +	+ +*	neg.	neg.	neg.

*Salicylic acid 5% vas. + +, Balsam of Peru pure neg.

secutive patients sensitive to the mixture of salicylic acid in lanolin, Thirty-five showed positive reactions to other patch tests with derivatives of lanolin such as wool alcohol etc, a total of twenty had positive reactions to creams of various types, while in only three cases the reactions could be discarded as irrelevant (Table XI.)

The material collected indicates that the patterns of sensitivity vary, as some patients show positive reactions to lanette wax, others to some aliphatic alcohols, some to eucerin and others not. As mentioned, several substances incorporating lanolin were included in our routine patch tests. Anti-oxidants have a capacity to neutralise the allergenic properties of lanolin (Table XII). If an anti-oxidant could abolish the allergenic properties of lanolin, the peroxides formed during storage might conversely be expected to accentuate them. Patch tests with eucerin stored in a tight jar for seven years confirmed this assumption, as shown by the findings presented in Table XIII.

TABLE XIII

COMPARISON OF PATCH TEST REACTIONS TO TWO DIFFERENT SAMPLES OF EUCERIN

		Eucerin (fresh)	
		Positive	*Negative*
Eucerin	Positive	11	9*
7 years old	Negative	0	0

*7 patients with negative reactions to fresh eucerin had positive reactions to other lanolin-tests : Parabens 14% or benzocaine 5% in eucerin c.aqua or to salicylic acid in lanolin.

Clinical Features

For the purposes of the present paper, I perused fifty case histories of consecutive patients sensitive to lanolin. The patients had been examined by routine patch test and, because of a positive or doubtful reaction to a substance in lanolin, they were tested with anhydrous wool fat or lanolin, that is, wool fat containing 30% water. The number of patients in the group according to their degrees of positive reaction is shown in Table XIV.

TABLE XIV

Reaction	*No. of Patients*
?	2
+	16
++	27
+++	4
++++	1
Total	50

Sensitivity to lanolin is most frequent in women and in elderly patients since only ten out of the fifty patients were under fifty years of age (Fig. 4). The maximal incidence was in the sixth and seventh decades. Most of the patients have a long history of eczema before the diagnosis of lanolin sensitivity is made (Fig. 5).

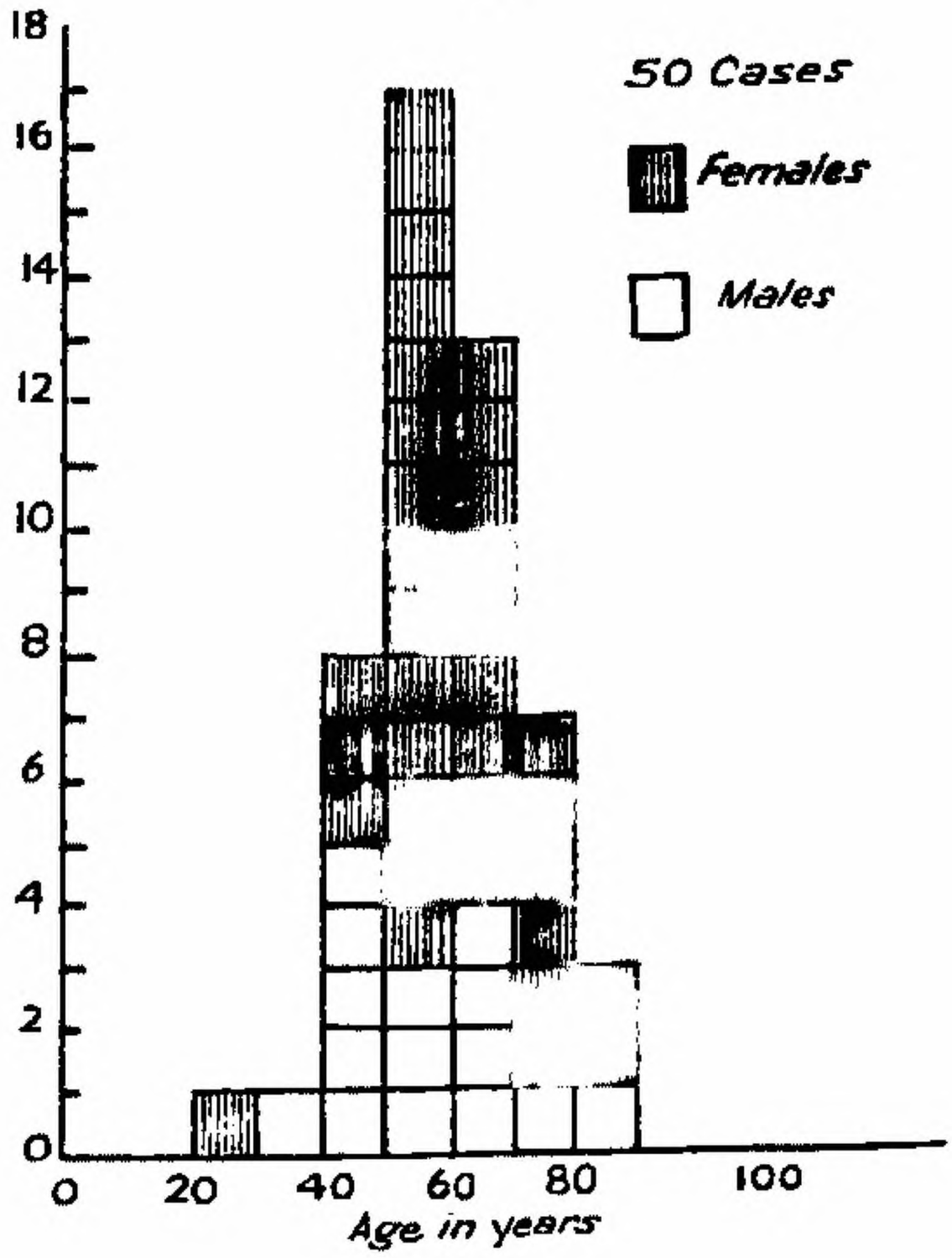

FIGURE 4
SENSITIVITY TO LANOLIN—AGE AND SEX INCIDENCE

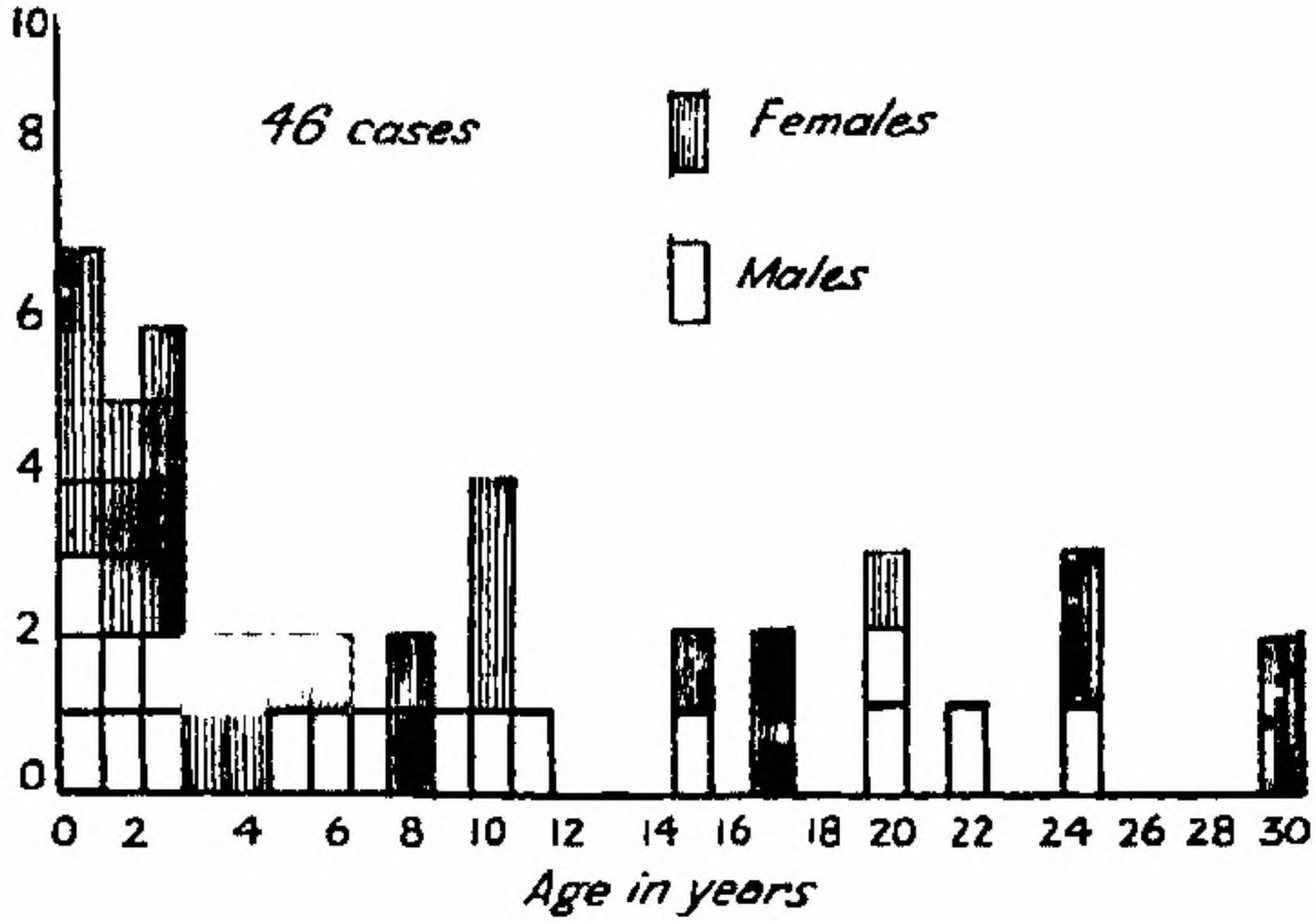

FIGURE 5
DURATION FROM FIRST ATTACK OF ECZEMA TO DIAGNOSIS OF SENSITIVITY TO LANOLIN

Both the preponderance of women and of elderly patients may be explained by the fact that sensitivity is particularly common in patients with varicose eczema (Fig. 6). This condition occurs especially in women and many of the patients have a particularly long history of eczema. They are inevitably treated over long periods with many topical applications likely to contain lanolin, by virtue of the chronic and relapsing nature of the condition.

Spread to secondary sites is very common in any type of therapeutic dermatitis, whether starting on the legs or in other regions. Especially puzzling are the cases which show little or no reaction in spite of the gradual spread of dermatitis. Of the thirty-seven patients showing spread to secondary sites, three showed no local aggravation while a further eight had but negligible local irritation, so that from a clinical point of veiw, there was little to indicate the true cause of the dermatitis. Id-like eruptions are frequent. In fact, we feel that the previous concept of auto-immunization as a cause of this type of eruption must be very rare indeed. In most patients studied at the Finsen Institute over the last few years, it has been possible to trace the cause of the id-like eruption to a sensitivity to topical medicaments. We find no clinical difference whether the eruption is caused by neomycin, parabens or lanolin.

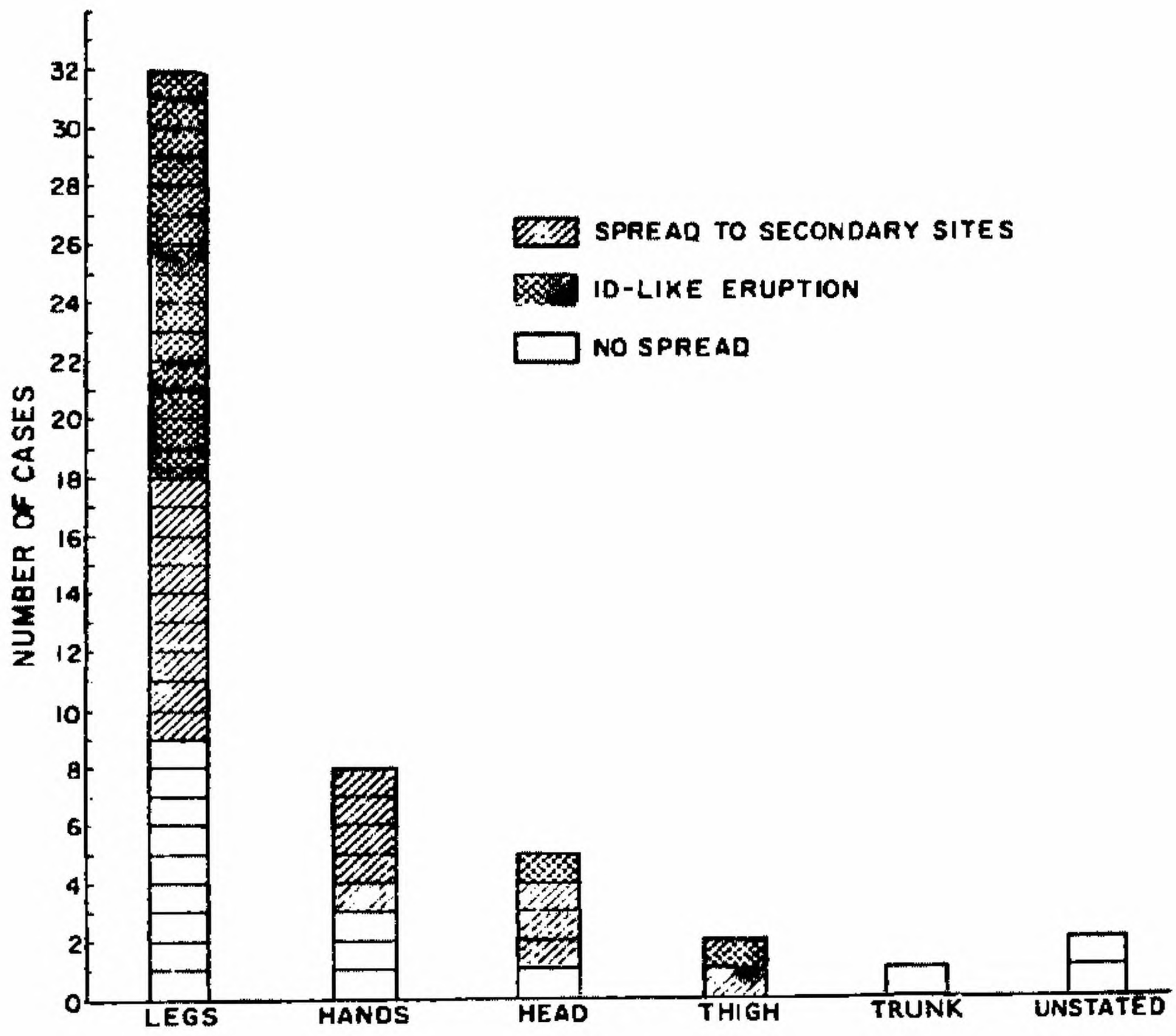

FIGURE 6

PRIMARY SITE OF ECZEMA IN 50 PATIENTS SENSITIVE TO LANOLIN

Sulzberger et al. (1953) has discussed whether sensitivity to lanolin might somehow be connected with auto-immunization and, in fact, this was what started his study in 1950. An eminent authority on the chemistry of lanolin, Truter of Leeds, has, however, refuted the idea as having no basis in the known facts of the chemistry of wool fats and sebum (Everall and Truter, 1954). We, therefore, maintain that so far the id-like spread from sensitivity to lanolin is no different from similar eruptions caused by other medicaments.

Patients with id-like eruptions are more likely than others to show non-specific reactions on testing. It should, however, be noted that most of the patients have reacted to several tests containing lanolin. Hence, if these positive reactions which occur in quite a logical manner should be considered primary irritant ones, we should have to introduce a new term, namely, a specific non-specific reaction. Sensitivity to lanolin rarely goes alone. Only seventeen out of the fifty patients had no other positive patch test, eleven had been tested for creams with positive results, while seven reacted to noemycin. Nine patients reacted to tars. Not all the patients have been thoroughly examined.

Relevance

In thirty-five out of the fifty patients the aggravation or attack of eczema which led to the Dermatology Department could be ascribed to the use of ointments containing lanolin. Some positive reactions found by routine patch testing may be irrelevant, but the figure of 70% relevant positive tests indicates that lanolin is a useful part of a series of routine patch tests.

Comment

The incidence of sensitivity to lanolin among the patients with eczema seen at the Finsen Institute is quite impressive, especially because a greater number of patients are examined there than in most other clinics.

Since only a fraction of patients with eczema suffer from dermatitis of the legs, the frequency of lanolin sensitivity among these is very high indeed. Conversely, lanolin sensitivity would be rare in a particular clinic where patients with eczema of the legs were not examined with a view to therapeutic sensitivities. The number of cases found will further depend upon the age group of patients attending a particular clinic.

To summarize, sensitivity to lanolin is frequent and extremely so in patients with eczema of the leg. It is a common cause of the so-called id-like eruptions and likely to be overlooked unless patch tests are performed with concentrates of lanolin allergen, such as wool alcohol or possibly with salicylic acid in lanolin.

Conclusions

Contact dermatitis from the classic dermatological remedies is in most cases unmistakable for a trained dermatologist. With the intrduction of steroid ointments, however, the clinical picture has changed.

1. The suppressive action of the steroid is capable of preventing a local reaction, but cannot prevent a gradual spread of dermatitis.
2. Sensitivity may manifest itself merely by a chronic course, without any acute flare or spread giving rise to a suspicion of dermatitis medicamentosa. This particular symptom, lack of improvement or failure to heal, is likely to be overlooked unless the dermatologist in charge of the patients' treatment is particularly alert to it.

Thus, it is not enough to test only such cases where the clinical picture is immediately suggestive of dermatitis medicamentosa. This observation is one of the major reasons for our use of routine patch tests without which we would probably have missed the majority of the sensitivities recorded in this paper.

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ADDENDUM

The sources of the substances used for patch tests were : Lanolin (Grade 2, Pharmaceutical) supplied by Westbrook Lanolin, England. Glyceryl monostearate, isopropylmyristate, and oleyl alcohol by Nordisk Droge & Kemikalie Co., Denmark. Octyl, decyl, lauryl, myristyl, cetyl, stearyl and cetostearyl alcohols by Aarhus Oliemolle, Denmark. Glyceryl Monostearate supplied by Marchon Products, England. Specifications of the substances used are available at request to the authors.