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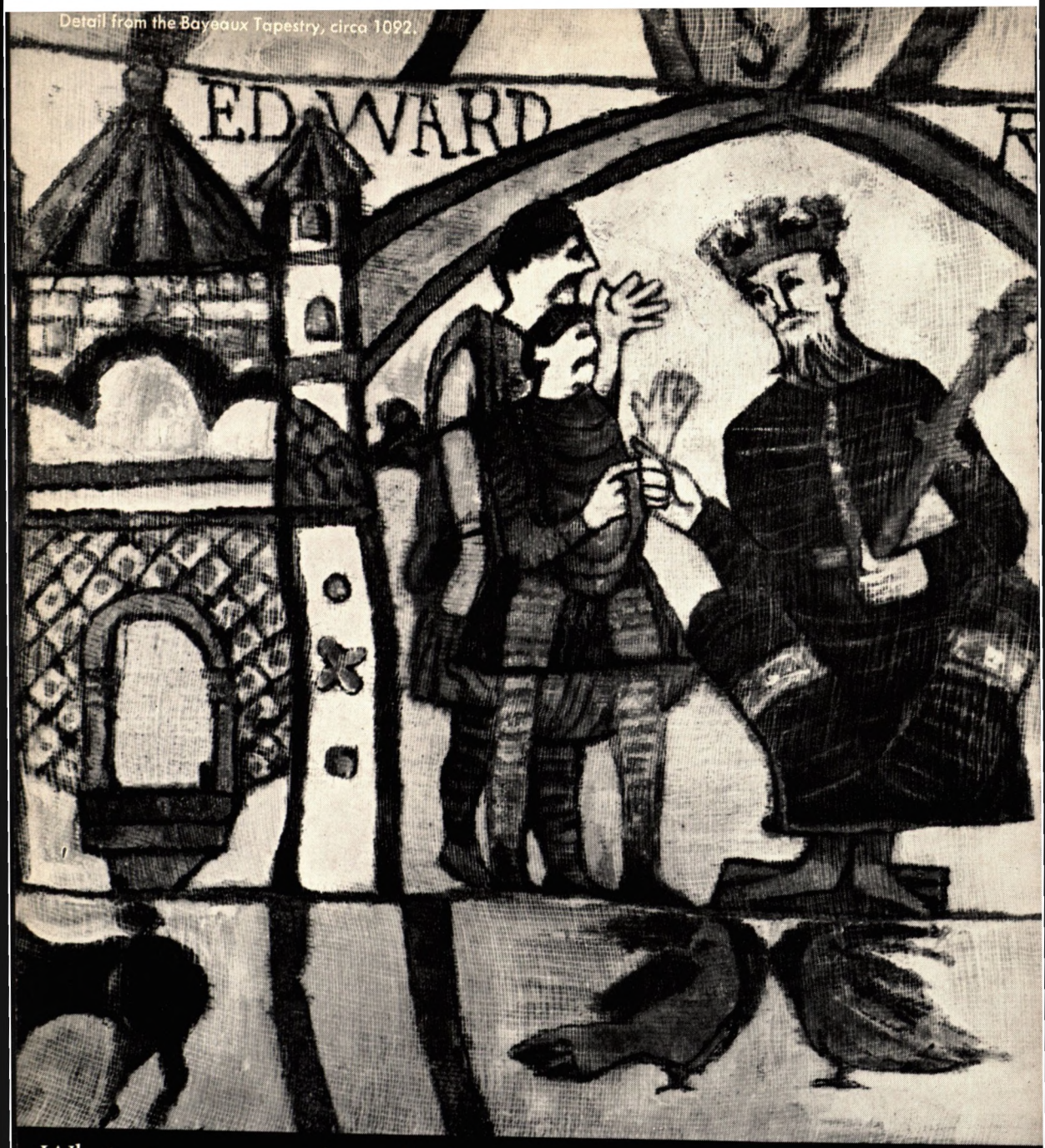

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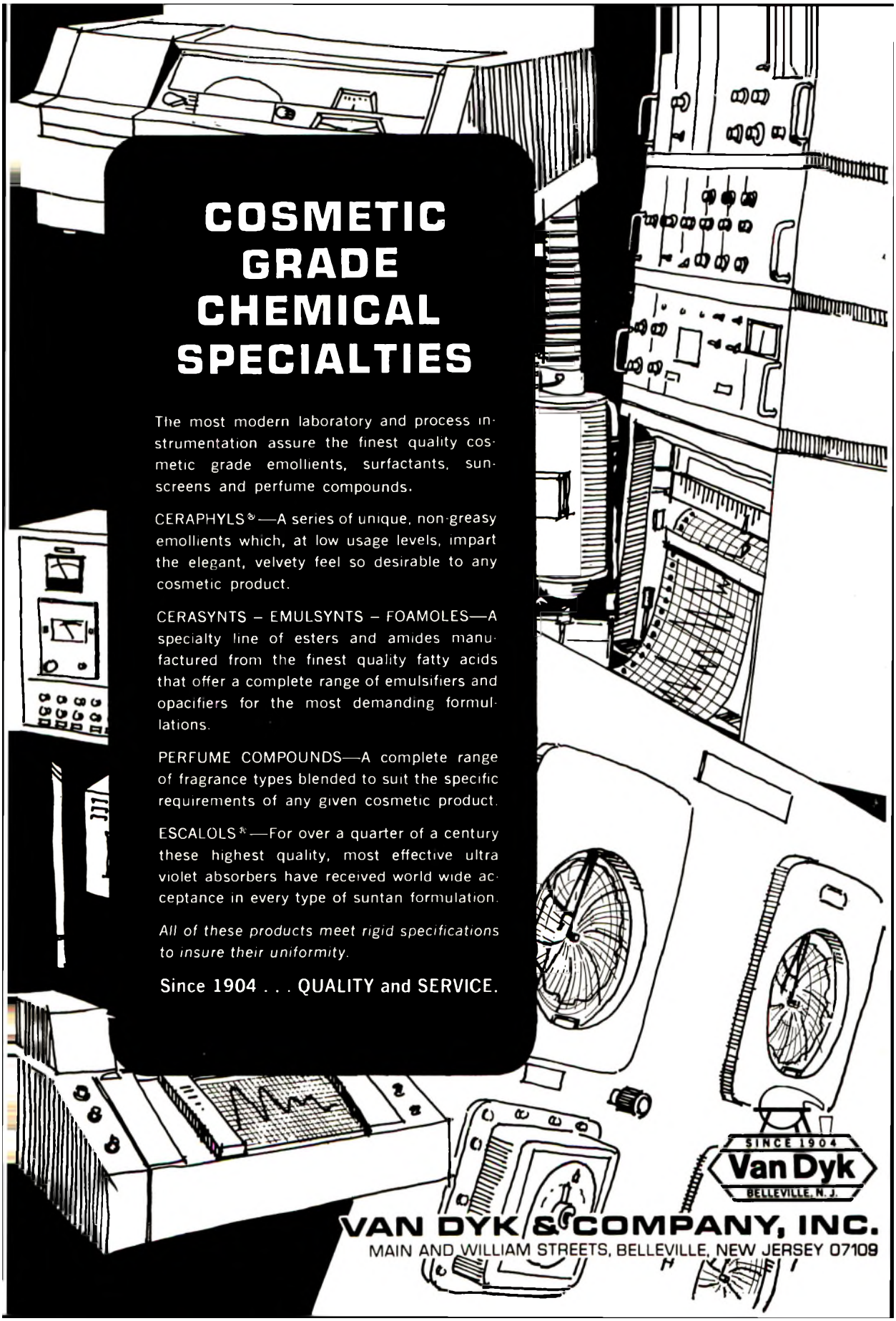

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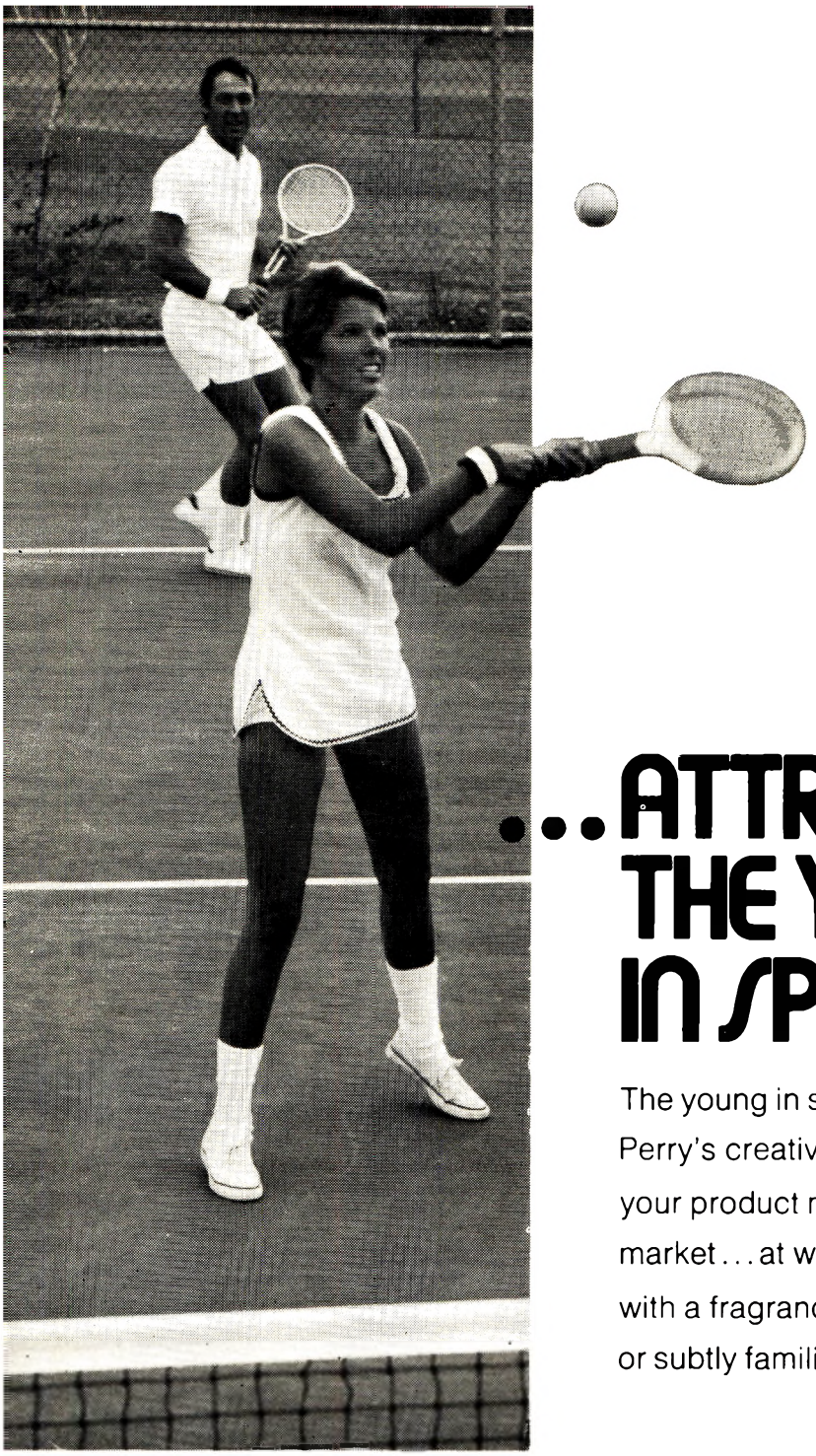

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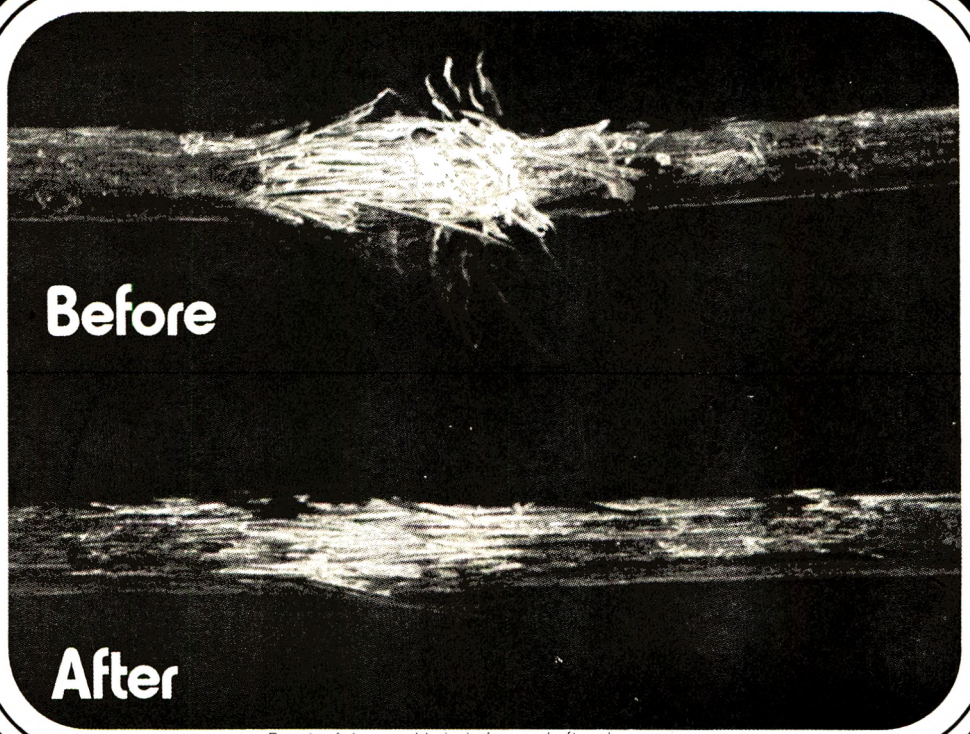

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The following synopses can be cut out and mounted on 3 x 5 in. index cards for reference, without mutilating the pages of the Journal.

Inhibition of palmar skin conductance in mice by antiperspirants and their relative anhidrotic activities: Rene Marcy and Marie-Anne Quermonne. *Journal of the Society of Cosmetic Chemists* **27**, 333 (August 1976)

Synopsis—In order to systematically test the anhidrotic activities of potential antiperspirants in relation to a standard or to cross-compare various formulations, an experimental method that uses mice was developed. The antiperspirant was applied to footpads with a rotating applicator which was gripped by mice; thus preventing the animals from removing it by grooming. The anhidrotic effect was evaluated by lowering palmar skin conductance. This was read with a conductance-meter built so that the mice themselves could grasp the electrodes by reflex action. Several topical anhidrotics were tested to determine the intensity, duration, and after washing persistence of their anhidrotic activity. The calculation of the concentrations, which inhibit sweating by 50 per cent (weight/volume and molar anhidrotic concentrations 50) and of the relative activities, allows the objective comparison of the anhidrotics. Reliability and utility of the test are discussed in this paper.

Potential and limitation of cosmetic safety testing on man: Erich Ludwig. *Journal of the Society of Cosmetic Chemists* **27**, 345 (August 1976)

Synopsis—Human testing is essential in order to eliminate sensitization by cosmetic products with a high degree of probability. In our opinion, the most frequently used and most reliable method is the repeated insult test according to Shelanski and Shelanski. Opponents of this procedure claim that it is a bodily insult which is subject to civil penalties. Arguments against this position are cited. The author stresses that, in the course of 15 years, no product which was declared safe on the basis of this test later elicited complaints due to allergic reactions.

A stereomicroscopic method for the determination of moisturizing efficacy in humans: Derek R. Highley, Vera O. Savoyka, John J. O'Neill, and John B. Ward. *Journal of the Society of Cosmetic Chemists* **27,** 351 (August 1976)

Synopsis—A stereomicroscopic test for moisturizing efficacy has been developed which is based upon the ability of moisturizers to prevent or alleviate soap-induced dry skin using the back of the hand as a substrate. The method is founded on objective definitions of the terms "dry skin" and "moisturizer." These definitions do not apply any particular etiology of the condition, nor do they imply any particular mechanism of efficacy in treatment.

One advantage of this procedure is that it permits comparative efficacy measurements on moisturizing preparations regardless of their form or water content. Another is, that by means of this test using panels of small size, information is generated, which could otherwise be obtained only through clinical testing on large populations.

A numerical grading system for relative skin dryness has been developed by means of which a numerical measure of moisturizing efficacy is obtained. Computerized statistical analysis of the data is performed when two materials are compared for moisturizing efficacy.

Clinical aspects of dry skin: Marvin E. Chernosky. *Journal of the Society of Cosmetic Chemists* **27,** 365 (August 1976)

Synopsis—Adequate prevention and management of dry skin problems are based on the prediction of establishing a correct diagnosis, a feat often not accomplished by patients and physicians. The incidence of dry skin symptons is increasing because of changes in the work and leisure time milieu of large portions of the population. Regulation of environmental exposure and patient education are important preventive measures. Specific methods for maintenance of stratum corneum water barrier and binder characteristics are unknown, but many topically applied formulations, sometimes in conjunction with systemic medications, restore the skin to normal appearance clinically and rid the patient of associated symptoms. The cosmetic chemist, physician, and user of dry skin products should be aware that adverse reactions to their topical use can occur.

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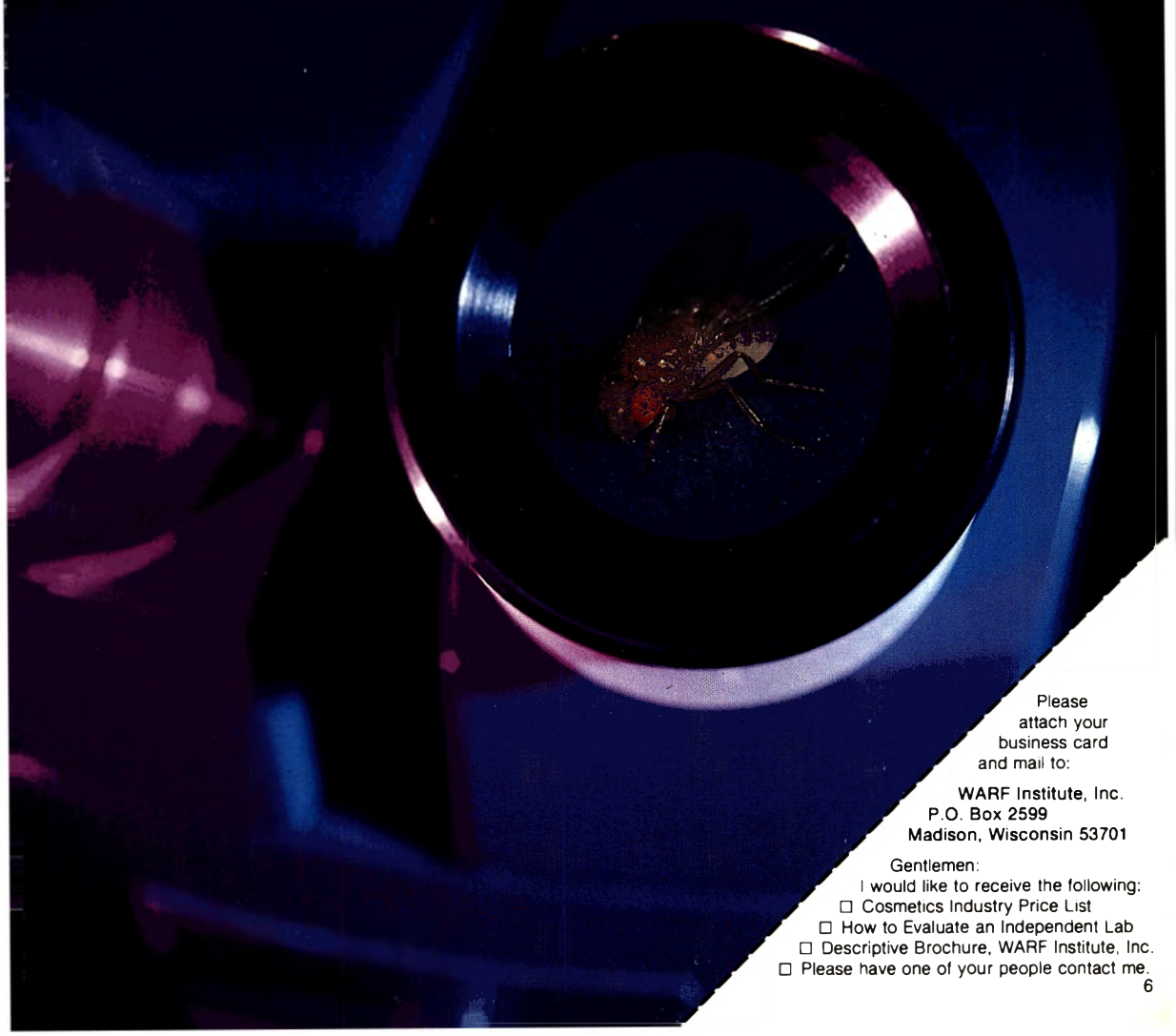

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J. Soc. Cosmet. Chem., **27**, 333-344 (August 1976)

Inhibition of palmar skin conductance in mice by antiperspirants relative anhidrotic activities

RENE MARCY, M.D., D. PHARM. and MARIE-ANNE QUERMONNE, D. PHARM.*

Synopsis—In order to systematically test the ANHIDROTIC ACTIVITIES of potential ANTIPERSPIRANTS in relation to a standard or to cross-compare various formulations, an experimental method that uses mice was developed. The antiperspirant was applied to footpads with a rotating applicator which was gripped by mice; thus preventing the animals from removing it by grooming. The anhidrotic effect was evaluated by lowering PALMAR SKIN CONDUCTANCE. This was read with a conductance-meter built so that the mice themselves could grasp the electrodes by reflex action. Several topical anhidrotics were tested to determine the intensity, duration, and after washing persistence of their anhidrotic activity. The calculation of the concentrations, which inhibit sweating by 50 per cent (weight/volume and molar anhidrotic concentrations 50) and of the relative activities, allows the objective comparison of the anhidrotics. Reliability and utility of the test are discussed in this paper.

Introduction

In testing antiperspirant formulations, different procedures may be used (1-5). A paper (6) concerned with skin conductance measurement failed to show any activity of locally applied aluminum salts, so doubt was cast on this type of method (2). However, we have recently developed (7-9) a method measuring palmar skin conductivity in mice in relation to palmar sweating. Consequently, this has been extended to antiperspirant testing, and a short preliminary note (10) has been published.

*Dermopharmacological Department, Pharmaceutical Sciences Unit and Institute of Dermobiology and Cosmetodynamics, The University, 14032 Caen-Cedex France.

Materials And Methods

Animals

Swiss Orl mice* were kept in our laboratory for 4 days. The animals were given a continuous water supply and a standard diet (standard rat food pellets number 103—UAR 91360†). Animals of both sexes were used indiscriminately because we had previously (8) established that males and females respond in a similar way. When their weight reached 16 to 20 g, the mice were randomized into groups of 10 or 20. A different group was used with each concentration of the chemical tested.

Antiperspirants

The following chemicals were used, dissolved in distilled water at the concentrations noted in brackets: tannic acid (1,000, 5,000, and 20,000); trichloracetic acid (500, 1,500, and 5,000), zinc chloride (1,000, 10,000, and 30,000); zinc phenolsulfonate (1,000 and 10,000), aluminum sulfate (1,000, 10,000, and 40,000); aluminum hydroxychloride (100, 500, 1,000 5,000, and 10,000); formaldehyde (500, 5,000, and 30,000); glutaraldehyde (780, 1,560, 6,250, and 25,000); and isopropamide iodide (100, 250, and 1,000). All concentrations are weight/volume (mg/100ml).

Mouse Palmar Skin Conductance Meter

A special apparatus, which has already been fully described (7-8), was used to evaluate the palmar skin conductance. The essential feature of this apparatus is the two electrodes, which are installed at a height of 17 cm above the work surface (Fig. 1). The dc current (4.5 V, 15 to 20 μA) is totally painless.

Topical Solutions Applicator

To apply the topical solutions to the palmar skin, we used a rotating applicator. This apparatus was comprised of a horizontal rod 30 mm in diameter and 180 mm in length; 4 plates perpendicular to the rod to divide it into 3 partitions. The rod was covered with 12 thicknesses of surgical gauze. From left to right, the 3 partitions were, respectively, treatment, washing, and drying partitions. The gauze in the first partition was soaked with a topical solution to be tested and the gauze in the second partition was soaked with distilled water. The gauze in the third partition was left dry. The rotating rod was turned by an electric motor at 17 rpm (Fig. 2).

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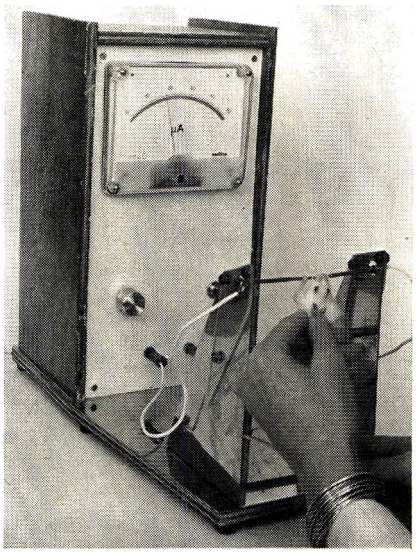

Figure 1. Reading of palmar skin conductance. Note way mouse is held and way it grasps electrodes

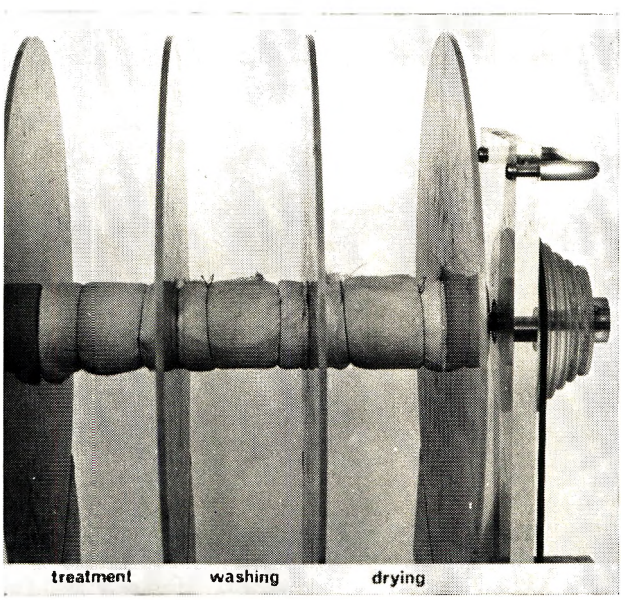

Figure 2. Antiperspirant applicator. Note division of rod into three sections; respectively, treatment, washing, and drying

Method

The first reading of the palmar skin conductance (r_0) was taken by placing a mouse held by its nuchal skin against the electrodes, which it immediately grasped (Fig. 1). The rotating rod was then switched on, and the mouse was placed on the rod in the treatment partition for 30 sec. During this time, due to the rod's rotation, the mouse was forced to run on the rod to avoid falling. Depending on the particular experimental schedule, the mouse was then either placed in the washing partition for 3 min, and in the drying partition for the same length of time, or placed directly in the drying partition.

New palmar skin conductance readings were taken 1, 4, 7, and, if necessary, 24 hours after treatment ($r_t = r_1$, r_4, r_7, and r_{24}). The anhidrotic activity for each animal at the time of each reading, was calculated by the formula $\frac{r_t - r_0}{r_0} \times 100$

The mean figure for a group, corresponding to a particular concentration, was then calculated. Whenever possible, the regression equation $y = a \log x + b$ (where y stood for palmar skin conductance the variation per cent and x stood for the logarithm of the concentration) was established. By taking y as -50 per cent, the corresponding value of x (i.e., the anhidrotic concentration, which lowered sweating by 50 per cent) was calculated. This figure was called anhidrotic concentration 50 and was determined in weight/volume (mg/100 ml) and in moles. The relative anhidrotic activities (weight/volume and molar relative anhidrotic activities) were calculated, taking the anhidrotic activities of aluminum hydroxychloride as 100 after 4 hours.

Reliability Tests

Saturated Na Cl solution was locally applied to 10 mice, without washing them, according to the above described method. A reading of palmar skin conductance was taken 15 and 30 min after application. Two batches of 10 mice were (intraperitoneally) dosed with atropine sudfate (2 mg/kg). Ten min later, palmar skin conductance was recorded and local treatment with either aluminum sulfate or glutaraldehyde was carried out. A new reading of palmar skin conductance was taken 10 min after this.

Results

Reliability of the Method

Palmar skin conductance was not altered by saturated Na Cl solution, which was applied in the same way as the anhidrotics, palmar skin conductance variations were 1.33 per cent (confidence limits P = 0.05: − 4.64, + 7.32)

Table I

Analysis of the Variance of Regression Equations
Palmar Skin Conductance Variation Per Cent/Concentration

	Source of Variation	Sum of Squares	df[a]	Variance	F	P	Significance
4-hour reading	LR[b]	11,392.00	1	11,392.00	19.52	<0.001	H S
Tannic acid	DR[c]	1,203.22	1	1,203.22	2.06	>0.05	N S
	R[d]	15,752.07	27	583.41			
	T[e]	28,347.29	29				
	LR	6,165.22	1	6,165.22	14.80	<0.001	H S
7-hour reading	DR	62.38	1	62.38	0.14	>0.20	N S
	R	11,243.34	27	416.42			
	T	17,470.94	29				
4-hour reading	LR	7,875.89	1	7,875.89	18.81	<0.001	H S
Trichloracetic acid	DR	97.27	1	97.27	0.23	>0.20	N S
	R	23,859.63	57	418.59			
	T	31,832.79	59				
	LR	4,332.01	1	4,332.01	6.40	<0.05	S
7-hour reading	DR	80.68	1	80.68	0.11	>0.20	N S
	R	38,534.28	57	676.04			
	T	42,946.97	59				
4-hour reading	LR	4,617.56	1	4,617.56	24.03	<0.001	H S
	DR	344.55	2	176.27	0.89	>0.20	N S
	R	6,916.32	36	192.12			
	T	11,878.43	39				
Aluminum	LR	9,734.23	1	9,734.23	22.27	<0.001	H S
hydroxychloride	DR	1,056.59	2	528.28	1.20	>0.20	N S
7 hour reading	R	15,733.08	36	437.03			
	T	26,523.90	39				
Aluminum sulfate	LR	24,558.25	1	24,558.25	23.46	0.001	H S
4-hour reading	DR	10.82	1	10.82	0.01	0.20	N S
	R	28,269.36	27	1,047.01			
	T	52,838.43	29				
4-hour reading	LR	3,824.16	1	3,824.16	7.06	<0.05	S
Formaldehyde	DR	571.67	1	571.67	1.05	>0.20	N S
	R	30,849.54	57	541.22			
	T	35,245.37	59				
	LR	6,140.17	1	6,140.17	11.66	<0.01	S
7-hour reading	DR	3.39	1	3.39	0.006	>0.20	N S
	R	29,992.83	57	526.19			
	T	36,136.39	59				
4-hour reading	LR	29,540.14	1	29,540.14	66.00	<0.001	H S
Glutaraldehyde	DR	204.86	2	102.43	0.22	>0.20	N S
	R	34,013.80	76	447.55			
	T	63,758.80	79				
	LR	27,242.88	1	27,242.88	59.72	<0.001	H S

(Table con't on next page)

Table I (con't)

	Source of Variation	Sum of Squares	df[a]	Variance	F	P	Significance
7-hour reading	DR	1,954.76	2	977.38	2.14	>0.20	N S
(Glutaraldehyde)	R	34,668.16	76	456.16			
	T	63,865.80	79				
4-hour reading	LR	4,798.82	1	4,798.82	11.39	<0.01	S
Isopropamide	DR	176.85	1	176.85	0.41	>0.20	N S
	R	11.371.32	27	421.16			
	T	16,346.99	29				
	LR	8,507.76	1	8,507.76	14.34	<0.001	H S
7-hour reading	DR	932.08	1	932.08	1.57	>0.20	N S
	R	16,017.21	27	593.23			
	T	25,457.05	29				

[a] Degrees of freedom.
[b] Linear regression.
[c] Deviation from regression.
[d] Residual variation.
[e] Total.

and 2.40 per cent (− 2.88, + 7.70) after 15 and 30 min, respectively.

When sweating was pharmacologically inhibited, local application of anhidrotics did not alter the corresponding level of palmar skin conductance.

Concentration of the Solutions and Anhidrotic Activity

With the exception of zinc derivatives, for which it was impossible to find any relation between concentration and palmar skin conductance variation, the palmar skin conductance inhibition of all chemicals tested related to concentration. In most cases, it was possible to calculate the regression equations "palmar skin conductance variation/per cent concentration," which were, in general, highly significant (Table I) and to draw the corresponding lines (Fig. 3). From the relative activities (Table II), it can be seen that aluminum hydroxychloride, tannic acid, and the anticholinergic drug isopropamide were the most effective topical anhidrotics tested.

Duration of the Anhidrotic Effect

The activities of aluminum hydroxychloride and isopropamide were greater 7 hours after application (369 and 455, respectively) than 4 hours after application (100 and 164, respectively). The reverse was true for the other products tested (Table II).

At the maximal concentration tested, and after 24 hours, the anhidrotic effect of tannic acid had become very weak. With aluminum hydroxychloride, slight anhidrotic effects (palmer skin conductance variation = − 19.26 per cent, P = 0.05 confidence limits = − 10.16 and −28.36 per cent) persisted,

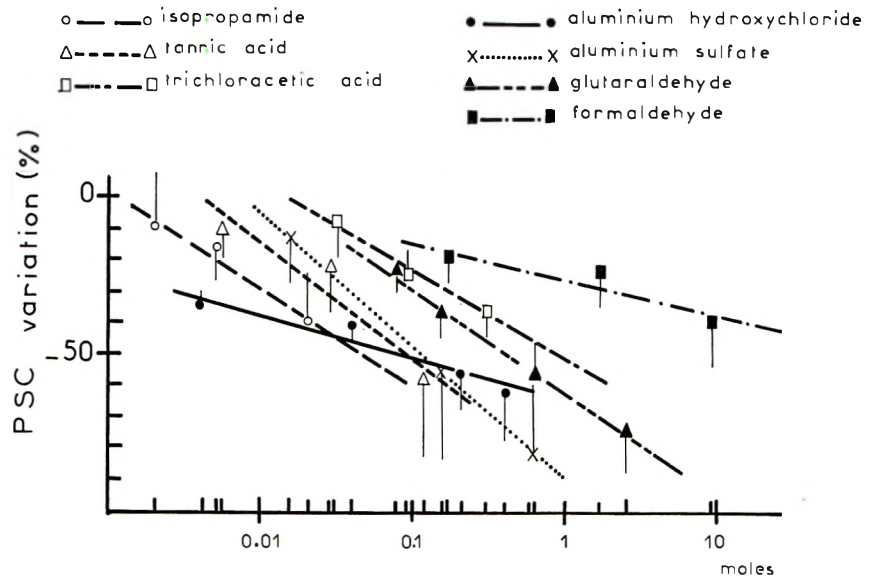

Figure 3. Regression lines "palmar skin conductance variation per cent/concentration" of various antiperspirants

Table II

Anhidrotic Concentrations 50 and Relative Anhidrotic Activities of Various Antiperspirants

Chemicals	Times of Readings (hours)	Weight/Volume (mg/100 ml) Anhidrotic Concentration 50	SE[a]	Relative Anhidrotic Activities	Moles x 10^{-4} Anhidrotic Concentration 50	SE[a]	Relative Anhidrotic Activities
Tannic acid	4	16,190	1,320	12	951	77	87
	7	25,500	1,640	8	1,498	96	55
Trichloracetic	4	14,770	350	13	9,039	214	9
acid	7	38,900	350	5	23,808	214	3
Aluminum	4	1,990	490	100[b]	824	202	100[b]
hydroxychloride	7	540	566	368	223	231	369
Aluminum sulfate	4	7,430	2,460	27	1,114	369	74
	7						
Formaldehyde	4						
	7	51,640	1,810	4	171,961	6,027	0.5
Glutaraldehyde	4	4,390	860	45	4,384	858	19
	7	6,360	820	31	6,351	818	13
Isopropamide	4	2,410	96	82	502	20	164
iodide	7	870	70	229	181	14	455

[a]Standard error of anhidrotic concentration 50 equals $\sqrt{\frac{Sx^2 - \frac{Sy^2}{n-2}}{n-2} \times \left(\frac{1}{n} + \frac{(-50 - \overline{Y})^2}{Sy^2}\right)}$,

$\overline{Y}$ is the mean palmar skin conductance variation per cent.

[b]Weight/Volume/ or molar activity of aluminum hydroxychloride equals 100.

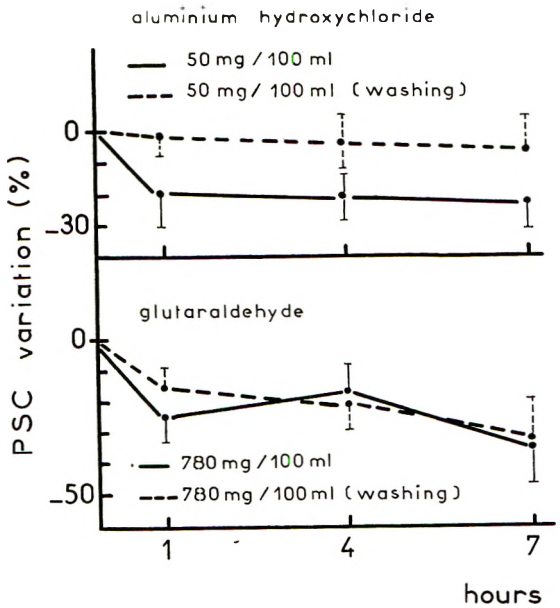

Figure 4. Effect of washing on palmar skin conductance variation after application of aluminum hydroxychloride and glutaraldehyde at certain concentrations

while in the case of glutaraldehyde, strong inhibition of palmar skin conductance could still be detected (palmar skin conductance variation = − 72.47 per cent. P = 0.05 confidence limits = −59.94 and −85.00 per cent).

Persistence of the Anhidrotic Action after Washing

At anhidrotic concentration 50 (1,990 and 4,390 mg/100 ml, respectively), the prewashing and postwashing anhodritic activities of aluminum hydroxychloride and glutaraldehyde remained identical. On the other hand, at minimal active concentrations (50 and 780 mg/100 ml), the topical anhidrotic action of aluminum hydroxychloride became zero if its application to the skin was immediately followed by washing, whereas, washing did not modify the anhidrotic action of glutaraldehyde (Fig. 4).

Discussion

The results obtained are consistent with research carried out to date. Trichloracetic acid was seen to be a poor anhidrotic (1); anticholinergic drugs (13, 14) and aldehydes (15, 16) to be active anhidrotics. Glutaraldehyde had a relatively long effect (15). Aluminum salts revealed themselves as good anhidrotics. Their antiperspirant effect reached a maximum 4 to 7 hours after application and was still perceptible after 24 hours (12). Aluminum

hydroxychloride was more active than aluminum sulfate at the same molar concentration.

Assessment of sweating by skin conductance is quite valid. The significative correlation (17, 18) and the linear relationship (19, 20) between skin conductance and sweating have been demonstrated. It is true that skin conductance is also dependent on epidermal cells (21, 22) and most certainly on the epidermal duct wall (23). However, in the present case, we have proved that mice palmar skin conductance was dependent on the excreted sweat, since palmar skin conductance increase due to pilocarpine was suppressed by drying footpad sweat (7).

The local blood flow (24-26) might interfere with skin conductance, whereas (27, 28), assert that this effect would be slight or even zero (29). In any case, it does not modify the skin conductance in this method, since intraperitoneally injected psycholeptics, without any vasoactivity, quantitatively inhibit palmar skin conductance; and, more importantly, adrenergic and adrenolytic drugs, which have contrary effects on vasomotricity, both inhibit palmar skin conductance (30, 31).

The possibility of a modification of palmar skin conductance by a physicochemical effect of the topical anhidrotic was ruled out by local treatment with saturated Na Cl solution. This did not alter the palmar skin conductance. Similarly, application of aluminium sulfate and glutaraldehyde on animals intraperitoneally pretreated by an anticholinergic drug was carried out in these conditions, the palmar skin conductance could only be modified by a physicochemical effect. There was no such modification.

So the inhibition of palmar skin conductance by a topical antiperspirant is, obviously, the consequence of its anhidrotic activity. As it has previously been demonstrated with intraperitoneally injected anticholinergic drugs (7), inhibition of palmar skin conductance by topical anhidrotics is related to dose, (i.e., the concentration of tested solutions). With active antiperspirants, the concentration response relationship may be expressed by a regression equation. Furthermore, the statistical calculation of anhidrotic concentration 50 affords an objective basis to the determination of the antiperspirant efficacy (weight/volume or molar standard anhidrotic activity), which is not obtained from an arbitrary choice of the concentrations tested.

So far, this has not been done. Either only semiquantitative results(variable number of positives) have been given (13, 32-35), when results have been expressed numerically (12, 15, 36-37), or graphically (38-40), no concentration-response equation was given except for (14). However, the latter method belongs to the quantal type (all or nothing response, i.e., sweating or no sweating)and thus affords less information than a quantitative method, i.e., based on a continuous variation of the effect (antiperspirant efficacy) according to dose (41), such as the one described here.

The method is not only quantitative, but also sensitive: the antiperspirant activity of concentration as low as 0.1, 0.5, and 0.78 for aluminum hydroxychloride formaldehyde, and glutaraldehyde, respectively, can be detected.

Since activity is not inferred from the duration of sweating after treatment as in (12), the duration of the anhidrotic effect can be recorded independently. In addition, the duration of the anhidrotic effect and its persistence, even after washing, are easily studied.

Use of the rotating rod for application of the topical anhidrotic takes the place of a tedious hand painting of the paws. As the mice have to grasp the rod, they are prevented from grooming and thus removing and absorbing the anhidrotic by mouth. The antiperspirant is applied on the skin, which is of much more practical interest than in (14), where chemicals tested were locally subcutaneously injected.

In contrast to (12, 37, 42), the effects are recorded in unanesthetized animals, and there is no need to stimulate sweating; thus excluding additional sources of error and simplifying (and shortening) the experimental schedule.

The use of mice to test antiperspirants developed for human subjects may meet with criticism (39), but such a procedure is the very basis of pharmacology. Tests on human volunteers have obvious drawbacks themselves (5). The use of the rat or mouse footpad for antiperspirant testing has already been advocated (12-14). Footpad sweat glands of mice belong to the eccrine type (43), as do human glands, and their pharmacological reaction is the same (7, 13, 43). Large, homogenous batches of mice are readily available, thus, allowing a rational design of experiments. Consequently, the test can be used to compare a series of potential antiperspirants to a standard or to cross-compare various formulations.

Acknowledgments

We are indebted to Mr. J. M. Elissalde for his technical assistance and to Mr. J. Scullard for helping to draft the text.

References

(1) R. Brum, Recherches sur la sécrétion sudorale et la sécrétion sébacée. Méthodes et expériences, *Arch. Sci.*, **7**, 243-302 (1954).
(2) T. A. Bakiewicz, A critical evaluation of the methods available for measurement of antiperspirancy, *J. Soc. Cosmet. Chem.*, **24**, 245-258 (1973).
(3) P. A. Majors and J. E. Wild, The evaluation of antiperspirant efficacy. Influence of certain variables, *J. Soc. Cosmet. Chem.*, **25**, 13-152 (1974).
(4) E. Jungermann, Antiperspirants : New trends in formulation and testing technology, *J. Soc. Cosmet. Chem.*, **25**, 621-38 (1974).
(5) R. Marcy, Antiperspirant efficacy testing: a critical review, *Cosmet. Perfum.*, **90**, 33-40 (1975).
(6) D. J. Perry, G. E. Mount, and J. Malimer, The effects of topically administered compounds on the galvanic skin response, *J. Invest. Dermatol.*, **36**, 7-9 (1961).
(7) R. Marcy, M. A. Quermonne, H. Marçais, and J. C. Chateau, Méthode d'évaluation quantitative rapide de la sécrétion sudorale palmaire chez la souris éveillée par mesure

de la conductivité électrique cutanée. Applications pharmacologiques dans le domaine cholinergique, *J. Pharmacol. (Paris)*, 4, 69-80 (1973).
(8) R. Marcy and M. A. Quermonne, An improved method for studying the psychogalvanic reaction in mice and its inhibition by psycholeptic drugs. Comparison with the effects of other pharmacological agents, *Psychopharmacologia*, 34, 335-49 (1974).
(9) R. Marcy and M. A. Quermonne, Anhidrotic effect of benzodiazepines in mice, *Experientia*, **30**, 783-4 (1974).
(10) R. Marcy and M. A. Quermonne, Comparaison de l'activité topique anhidrotique de trois dérivés de l'aluminium chez la souris, *Ann. Dermatol. Syphiligrie*, **101**, 288-90 (1974).
(11) C. M. Papa, The action of antiperspirants, *J. Soc. Cosmet. Chem.*, **17**, 789-800 (1966).
(12) A. B. G. Lansdown, The rat footpad as a model for examing antiperspirants, *J. Soc. Cosmet. Chem.* 24, 677-84 (1973).
(13) J. Sivadjian, M. Vautrin, and H. Vautrin-Matge, Action anhidrotique locale comparée de deux antichlinergiques, *Thérapie*, 22, 1015-20 (1967).
(14) E. Kaszynski and S. B. Frisch, Mouse foot screen for the inhibition of sweating by anticholinergic drugs, *J. Invest. Dermatol.*, 62, 510-13 (1974).
(15) L. Juhlin and H. Hansson, Topical glutaraldehyde for plantar hyperhidrosis, *Arch. Dermatol.*, 97, 327-30 (1968).
(16) M. Uttley, Measurement and control of perspiration, *J. Soc. Cosmet. Chem.*, 23, 23-43 (1972).
(17) R. C. Wilcott, Palmar skin sweating versus palmar skin resistance and skin potential, *J. Comp. Physiol. Psychol.*, 55, 327-31 (1962).
(18) R. C. Wilcott, Arousal sweating and electrodermal phenomena, *Psychol. Bull.*, **67**, 58-72 (1967).
(19) C. W. Darrow, The significance of skin resistance in the light of its relation to the amount of perspiration, *J. Gen. Psychol.*, **11**, 451-2 (1934).
(20) P. E. Thomas and I. M. Korr, Relationship between sweat gland activity and electrical resistance of the skin, *J. Appl. Physiol.*, **10**, 505-10 (1957).
(21) C. P. Richter, Physiological factors involved in the electrical resistance of the skin, *Amer. J. Physiol.*, **88**, 596-615 (1929).
(22) R. Edelberg and D. J. Wright, Two galvanic skin response effector organs and their stimulus specificity, *Psychophysiology*, **1**, 39-47 (1964).
(23) P. H. Venables and M. J. Christie, *Electrodermal activity in psychological research*, W. E. Prokasky and D. C. Raskin, ed., Academic Press, Oxford, 1973, Pp. 1-124.
(24) F. Aveling and R. J. S. McDowall, The effect of the circulation on the electrical resistance of the skin, *J. Physiol. (London)*, **60**, 316-21 (1925).
(25) H. B. Densham and H. M. Walls, The mechanism by which the electrical resistance of the skin is altered, *Quart. J. Exp. Physiol. Cog. Med. Sci.*, **18**, 175-84 (1927).
(26) A. Woolley-Hart, The role of the circulation in measurements of skin conductivity, *British J. Dermatol.*, 87, 213-226 (1972).
(27) R. C. Wilcott, Effects of local blood removal on skin resistance and potential, *J. Comp. Physiol. Psychol.*, **51**, 295-300 (1958).
(28) K. J. Collins, F. Sargent, and J. S. Weiner, Excitation and depression of eccrine sweat glands by acetylcholine acetyl-β-methylcholine and adrenaline, *J. Physiol. (London)*, **148**, 592-614 (1959).
(29) B. J. Prout, Independence of the galvanic skin reflex from the vasoconstrictor reflex in man, *J. Neurol. Neurosurg. Psychiat.*, **30**, 319-24 (1967).
(30) R. Marcy and M. A. Quermonne, Lowering of palmar skin conductivity in mice by ephedrine, *IRCS (Pharmacol. Drugs acting on the Autonomic Nervous System)*, 73-**4**, 7-8-5 (1973).
(31) R. Marcy and M. A. Quermonne, Quantitative inhibition of palmar sweating in mice by α-adrenolytic drugs, *IRCS (Neurohiol. Neurophysiol. Basic Pharmacol.)*, 2, 1022 (1974).
(32) J. Sivadjian, M. Vautrin, and H. Matge, Propriétés neuroleptiques et anhidrotiques du tripéridol (R.2498). Etudes pharmacologiques et hygrophotographiques, *Therapie*, 18, 1279-85 (1963).

(33) J. Sivadjian, M. Vautrin, and H. Vautrin-Matge, Etudes néurophysiologiques sur la sécrétion sudorale. Introduction à l'hidropharmacologie, *Thérapie,* **20,** 1389-1402 (1965).
(34) J. Sivadjian, Hygrophotographische Untersuchungen kosmetischer Mittel insbesondere Antihidrotike, *Parfüm. Kosmet,* **46,** 162-6 (1965).
(35) M. M. Blozovski and J. Sivadjian, Action de la sérotonine, de la réserpine et d'autres agents pharmacologiques sur la sécrétion sudoral. Etudes hygrophotographiques, *Arch. Int. Pharmacodyn. Ther.,* **123,** 58-66 (1959).
(36) G. W. Fredell and J. Longfellow, Evaluating antiperspirant and deodorant products, *J. Soc. Cosmet. Chem.,* **9,** 108-11 (1958).
(37) R. S. Alphin, J. A. Vecac, D. Saunders, and J. W. Ward, Effects of some lignosulfonates on sweat gland activity, *J. Pharm. Sci.,* **58,** 902-3 (1969).
(38) E. G. Helton, E. W. Daley, and J. C. Ervin, Zirconium oxychloride a new ingredient for antiperspirants, *Proc. Sci. Sect. Toilet Goods Ass.,* **26,** 27-31 (1956).
(39) R. J. James, A new and realistic electronic approach to the evaluation of antiperspiran activity, *J. Soc. Cosmet. Chem.* **17,** 749-67 (1966).
(40) A. Winkler, Zur Methodik der Testung von Antitranspirantien, *Fette Seifen Anstrich.,* **70,** 893-5 (1968).
(41) D. J. Finney, *Statistical Method in Biological Assay,* Ch. Griffin Ltd., London, 1952, p. 58.
(42) R. S. Alphin, D. Saunders, and J. W. Ward, Method for the evaluation of anhidrotic substances in the anesthetized cat, *J. Pharm. Sci.* **56,** 449-52 (1967).
(43) H. Hayashi, Functional activity of the sweat glands of the mouse, *Tohoku J. Exp. Med.,* **95,** 289-95 (1968).

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Möglichkeiten und Grenzen der Prüfung von Kosmetika auf Verträglichkeit am Menschen

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Vorgetragen am 22. Mai 1975 in Varna/Bulgarien anläßlich der 2. nationalen Konferenz über Probleme der kosmetischen und Parfümerie-Industrie

Synopsis — Potential and limitation of cosmetic safety testing on man. — Human testing is essential in order to eliminate sensitization by cosmetic products with a high degree of probability. In our opinion, the most frequently used and most reliable method is the repeated insult test according to Shelanski and Shelanski. Opponents of this procedure claim that it is a bodily insult which is subject to civil penalties. Arguments against this position are cited. The author stresses that, in the course of 15 years, no product which was declared safe on the basis of this test later elicited complaints due to allergic reactions.

Das Lebensmittel-Gesetz der Bundesrepublik Deutschland, dem auch die Kosmetika unterstehen, besagt, daß es verboten ist, Erzeugnisse herzustellen und zu vertreiben, die bei bestimmungsgemäßer Anwendung die menschliche Gesundheit schädigen können. Ähnliche gesetzliche Bestimmungen gibt es in fast allen Ländern.

Eine Gesundheitsschädigung durch Kosmetika, die kurzfristig oder auch über längere Zeit mit der menschlichen Haut oder Mundschleimhaut in Berührung kommen, kann dadurch erfolgen, daß

1. ein bestimmter Bestandteil des Produktes resorbiert wird und im Organismus toxisch wirkt,
2. das Produkt die Haut primär reizt
   oder
3. zu einer Sensibilisierung führt.

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Der Nachweis der Toxizität eines Stoffes stellt im allgemeinen kein Problem dar, zumal sie im Tierversuch leicht möglich ist. Die tierexperimentell nachgewiesene Toxizität eines Stoffes schließt übrigens dessen Einsatz in Kosmetika nicht automatisch aus. Man denke nur an die in Dauerwellflüssigkeiten enthaltene Thioglykolsäure. Bei bestimmungsgemäßer Anwendung wird der an sich toxische Stoff nicht oder in pharmakologisch nicht relevanten Mengen resorbiert.

Auch die Frage, ob ein Stoff die menschliche Haut reizen wird, läßt sich im Tierversuch, namentlich wenn dieser an mehreren Spezies durchgeführt wird, mit ausreichender Sicherheit beantworten.

Im Gegensatz zur Toxizität und zur Reizwirkung ist die Sensibilisierung ein Risiko, das im Tierversuch allein nicht ausgeschlossen werden kann. Mit anderen Worten: Selbst wenn das Meerschweinchen, das für Allergie-Versuche am meisten geeignete Tier, durch einen Stoff nicht sensibilisiert worden ist, so schließt das die Möglichkeit der Sensibilisierung des Menschen nicht aus. Eine Prüfung des Sensibilisierungsvermögens am Menschen selbst ist daher unerläßlich.

Die Prüfung an der menschlichen Haut ist möglich in der Form der einfachen epicutanen Testung mittels Läppchenprobe (patch test) an freiwilligen Probanden oder aber durch die praktische Anwendung, die dem beabsichtigten Gebrauch entspricht.

Von den bekannten Testmethoden, die etwas über das Sensibilisierungsvermögen einer Zubereitung oder eines Stoffes aussagen, ist mit Abstand der sog. repeated insult patch-Test von Shelanski u. Shelanski (2) der zuverlässigste. Die Bezeichnung ist nicht ganz glücklich, denn das Wort „insult" verleitet zu der Annahme, daß die Haut skarifiziert oder sonstwie geschädigt wird, was nicht der Fall ist. Bei dieser Methode, die einerseits leider nicht genügend bekannt ist, sich mir aber andererseits im Laufe von Jahren optimal bewährt hat, wird eine bestimmte Menge der zu testenden Substanz auf ein Testpflaster gebracht und dieses für 24 Stunden auf die unvorbehandelte und unbeschädigte Haut des Probanden appliziert.

Nach 24 Stunden wird das Testpflaster abgenommen und die Reaktion abgelesen. Nach einer Pause von 24 Stunden, also insgesamt 48 Stunden nach der Pflasterapplikation erfolgt eine zweite Ablesung. Anschließend wird ein neues Testpflaster genau auf das Hautareal appliziert, auf dem schon das erste Pflaster gelegen hat. Dieser Vorgang wird mehrfach wiederholt. Nach der ursprünglichen Empfehlung von Shelanski u. Shelanski 14mal, nach der Empfehlung der Deutschen Gesellschaft für Fettwissenschaften (1) 5mal. Ich selbst wiederhole die Pflasterapplikationen 8mal. In jedem Fall erfolgt nach den wiederholten Applikationen eine Pause von mehreren Tagen. Diese beträgt

bei Shelanski u. Shelanski 2—3 Wochen, bei der Deutschen Gesellschaft für Fettwissenschaften 10 Tage. Ich selbst lege auch eine Pause von 10 Tagen ein. Nach dieser Zeit erfolgt die sog. auslösende Testung an einem bis dahin unbehandelten Hautareal, die über eine möglicherweise eingetretene Sensibilisierung Aufschluß geben soll.

Eine Reaktion nach der ersten Applikation besagt, daß der zu prüfende Stoff primär reizt oder daß der Proband gegen denselben bereits sensibilisiert ist. Weitere Pflasterapplikationen erfolgen in solchen Fällen nicht mehr. Eine später im Verlaufe der mehrwöchigen Testperiode auftretende positive Reaktion zeigt an, daß eine Hautermüdung (skin fatigue) eingetreten ist. Es handelt sich hier um eine Reaktion durch Kumulierung unterschwelliger Reize. Die positive Reaktion kann aber auch besagen, daß eine Sensibilisierung eingetreten ist. Zur Klärung der Frage, ob es sich um eine allergische Reaktion oder um eine Hautermüdung handelt, erfolgt die nächste Pflasterapplikation auf einem unmittelbar benachbarten Hautareal. Fällt die Reaktion wieder positiv aus, vielleicht sogar noch stärker positiv als die vorausgegangene, so beweist das eine in der Zwischenzeit eingetretene Sensibilisierung. Ein negativer Test im Bereiche des benachbarten Hautareals besagt, daß es sich nur um eine Hautermüdung gehandelt hat.

Die auslösende Testung 10 oder mehrere Tage nach dem Abstand von 2 Tagen wiederholten Pflasterapplikationen beantwortet die wichtige Frage, ob eine Sensibilisierung eingetreten ist oder nicht. Eine positive Reaktion, die erstmalig bei der auslösenden Testung auftritt, ist allergisch und liefert den Beweis für eine eingetretene Sensibilisierung.

Das soeben beschriebene Verfahren gestattet in einem Arbeitsgang den Nachweis primär reizender, hautermüdender und sensibilisierender Eigenschaften.

Gegen dieses Verfahren, das von der US-amerikanischen Food and Drug Administration wegen seiner hohen Aussagekraft akzeptiert wird, wenn es an mindestens 50 Probanden durchgeführt worden ist, werden von verschiedenen Autoren Einwände erhoben. Es wird behauptet, daß die mögliche Sensibilisierung eines Probanden eine Körperverletzung und somit eine strafbare Handlung darstelle. Dem ist entgegenzuhalten, daß

1. von einer Körperverletzung nicht die Rede sein kann, wenn die Testung mit Zustimmung des zuvor entsprechend aufgeklärten und bezahlten Probanden erfolgt,
2. die gegebenenfalls eingetretene Sensibilisierung im denkbar frühesten Stadium erkannt wird und daher zu erwarten steht, daß die auf diesem Wege erworbene Allergie nach kurzer Zeit wieder er-

lischt (entsprechende katamnestische Untersuchungen sind im Gange),

3. diejenigen, die ein solches Verfahren ablehnen, keine vernünftige Alternative zu bieten haben.

Verzichtet man auf jegliche Prüfung der Verträglichkeit am Menschen bzw. beschränkt sich auf eine einfache Epicutantestung, die über ein Sensibilisierungsvermögen überhaupt nichts aussagt, so kann das katastrophale Folgen haben. Ende der fünfziger Jahre hat eine ungenügend auf ihre Verträglichkeit geprüfte Dauerwellflüssigkeit zu einer wahren Epidemie an Berufsekzemen bei Friseuren geführt.

Ersetzt man die Prüfung auf sensibilisierende Eigenschaften mit Hilfe einer Testung im engeren Sinne (wiederholte Applikation von Testpflastern) durch einen sogenannten Expositionstest oder Gebrauchstest, so ist die Gefahr einer Sensibilisierung, die man vermeiden möchte, keineswegs ausgeschlossen. Da eine solche Prüfung in der Regel an einem größeren, weniger gut überschaubaren Kollektiv ohne unmittelbare ärztliche Kontrolle erfolgt, ist das Risiko einer Sensibilisierung noch viel größer. Durch die großflächige Applikation eines letztlich potentiellen Allergens ist die Möglichkeit einer massiven Sensibilisierung gegeben, die voraussichtlich lange anhält und unter ungünstigen Bedingungen sogar unerkannt bleiben kann.

Shelanski u. Shelanski betonen, daß Stoffe, die den von ihnen vorgeschlagenen Test bestanden haben, sich später bei ihrem Einsatz in Kosmetika in keinem Fall als unverträglich erwiesen haben. Aufgrund meiner in mehr als 15 Jahren gesammelten Erfahrung kann ich bestätigen, daß kein Produkt, das nach einer Prüfung im repeated insult patch-Testverfahren freigegeben wurde, später zu einer Reklamation wegen Unverträglichkeit Anlaß gegeben hat.

Zusammenfassung

Um sensibilisierende Eigenschaften eines kosmetischen Produktes mit einem hohen Grad an Wahrscheinlichkeit ausschließen zu können, ist eine Testung am Menschen selbst unerläßlich.

Für die bewährteste und zuverlässigste Methode halten wir den repeated insult patch-Test nach Shelanski u. Shelanski.

Gegner dieses Verfahrens behaupten, hier handle es sich um eine Körperverletzung, die strafbar ist. Es werden Argumente gegen die Berechtigung dieses Vorwurfes aufgeführt. Der Verfasser betont, daß im Verlauf von fünfzehn Jahren kein Produkt, das aufgrund dieses Prüfungsverfahrens freigegeben wurde, später zu Reklamationen wegen allergischer Reaktionen Anlaß gegeben hat.

Literatur

1. Empfehlungen für Hautverträglichkeitsprüfungen von Körperpflegemitteln (Kosmetische Erzeugnisse). Gemeinschaftsarbeiten der DGF: 54. *Mitteilung Fette, Seifen, Anstrichmittel* **73**, 467—469 (1971).

2. Shelanski, H. A. and Shelanski, M. V., A new technique of human patch tests, *Proc. Sci. Sect. Toilet Goods Ass.* **19**, 46—49 (1953).

A MESSAGE FROM THE EDITOR OF THE JSCC

As you know, The Journal of the Society of Cosmetic Chemists, along with all other publications, has been faced with increasing production costs over the past year. The cost of paper along with printing costs have increased to the point where some action must be taken in order to insure the continued scientific and technical integrity of The Journal. The Publications Committee has been considering this problem for the past several years and has found it necessary to increase its subscription rate to non-members, increase its advertising rates as well as to increase the total number of pages of advertising copy. We have now reached the point where we can no longer increase the number of advertising pages without proportionally increasing the number of pages devoted to scientific and technical articles. To do so would drastically change the nature of our Journal to the point where it would lose much of its professional status.

Therefore, in order to increase the number of pages devoted to scientific and technical papers, the Board of Directors have approved the institution of a modest page charge to be assessed each author of a published paper. While these page charges will be waived by the business office in cases of undo hardship, it is expected that sufficient income will be received so as to insure the continued viability of scientific and professional journals.

If we recognize that publication is one of the goals of research, then the cost of publication should be included as part of the research funding.

Sincerely,
John J. Sciarra, Ph.D.
Editor

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A Stereomicroscopic Method For The Determination Of Moisturizing Efficacy In Humans

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Presented, May 30, 1976, SCC Annual Seminar, St. Louis, Mo.

Synopsis: A Stereomicroscopic Test for Moisturizing Efficacy has been developed, which is based upon the ability of moisturizers to prevent or alleviate soap-induced dry skin using the back of the hand as a substrate. The method is founded on objective definitions of the terms "dry skin" and "moisturizer." These definitions do not apply any particular etiology of the condition, nor do they imply any particular mechanism of efficacy in treatment.

One advantage of this procedure is that it permits comparative efficacy measurements on moisturizing preparations regardless of their form or water content. Another is, that by means of this test using panels of small size, information is generated, which could otherwise be obtained only through clinical testing on large populations.

A numerical grading system for relative skin dryness has been developed by means of which a numerical measure of moisturizing efficacy is obtained. Computerized statistical analysis of the data is performed when two materials are compared for moisturizing efficacy.

Introduction

The influence of moisturizing agents on the status of stratum corneum water has been the subject of numerous publications. Water vapor transmission

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across isolated stratum corneum and *in vivo* measurement of transepidermal moisture loss have been used by several authors as an index of moisturizing efficacy (1, 2, 3, 4, 5, 6). Laden and Morrow (7), Park and Baddiel (8, 9), and Reiger and Deem (6, 10) studied the rheology of the stratum corneum in relation to its water content. The water binding capacity of the stratum corneum has been thoroughly investigated (11, 12, 13, 14). The efforts of the above investigators have stimulated research on moisturization and increased our knowledge concerning the dynamics of stratum corneum water. However, these techniques are not suitable for screening large numbers of ingredients and cosmetic formulations for moisturizing efficacy, for reasons which will be discussed later. Additionally, they do not directly relate to the signs of dry skin, familiar to many consumers.

Johnson *et al.* (15) and Gibson (16) in clinical studies, developed rating systems for determining the severity of dryness of volunteers' hands. Scaling, cracking, and redness were used as criteria of dryness. Because the parameters studied by Johnson *et al.* and Gibson relate directly to the signs of dry skin as they are experienced by the consumer, their use in the assay of moisturizers designed to combat this problem is indicated.

The subject of the present paper is the development of a stereomicroscopic test for moisturizing agents, which is based upon their ability to overcome soap-induced dry skin, using the back of the hand as the substrate. The following definitions are fundamental to the development of this technique.

1. Dry skin is a condition characterized by the presence of upraised edges of groups of stratum corneum cells, which reflect or refract light in a manner that is different from normal skin.
2. A moisturizer is an ingredient or product which prevents or alleviates the signs of dry skin.

By means of the procedure described here, any type of ingredient or formulation can be tested, regardless of water content, using relatively small panels of individuals who are prone to the development of dry skin. This permits the ranking of ingredients or products in order of their effectiveness and head to head comparison of two or more products for moisturizing efficacy.

Results obtained using the stereomicroscopic procedure have been corroborated by an independent testing laboratory.

Experimental Design and Results

I. *Stereomicroscopic Evaluation of Hands*

It is essential that one uses trained observers for the stereomicroscopic evaluation of dryness. It has been our experience that up to 3 weeks of training may be required before dependable results are obtained.

Table I
Definitions of Stereomicroscopic Dryness Ratings

0 = Normal skin, no observable scale at 30 X magnification.
1 = Occasional scale, not necessarily distributed uniformly, on either plateaus or sulci.
2 = Scale in sulci and on plateaus.
3 = Pronounced scaling visible to the naked eye, giving the surface a whitish appearance. Hand is rough to the touch.
4 = More scale with pronounced separation of scale edges. Some evidence of cracking in the sulci.
5 = Abundant scale, extensive cracking of the skin surface.

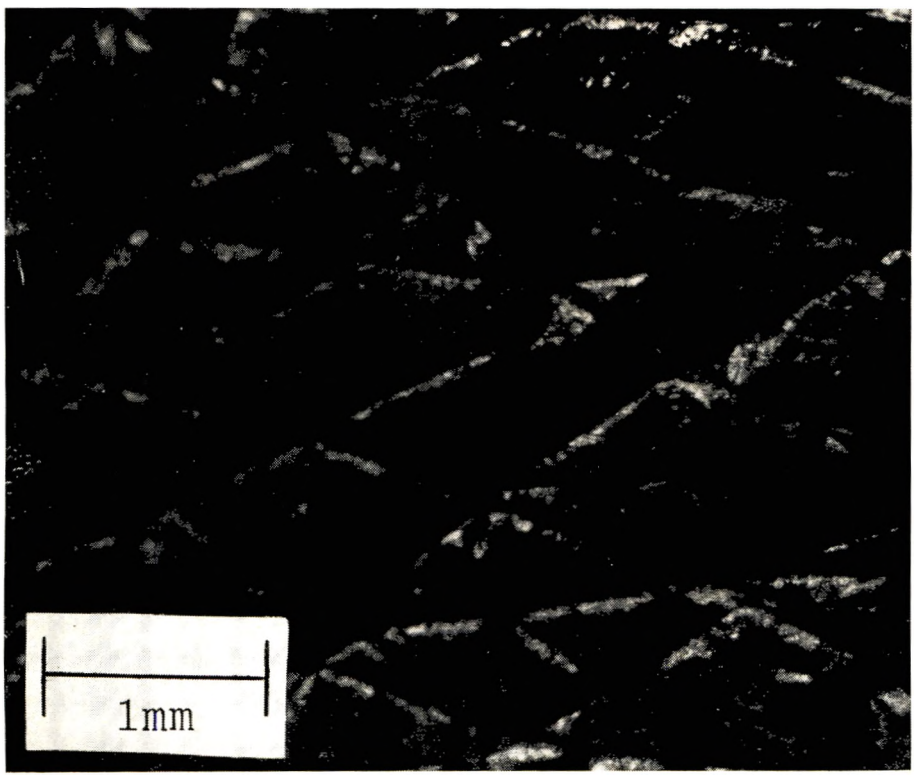

Figure 1. Optical photomicrograph of normal skin (zero dryness rating)

The back of the hand is scanned from the wrist to the knuckles with the stereomicroscope at 30X magnification. The hand is illuminated by means of a microscope lamp mounted on the stereomicroscope at a 30° angle to the skin surface. The dryness rating is mentally averaged according to the overall

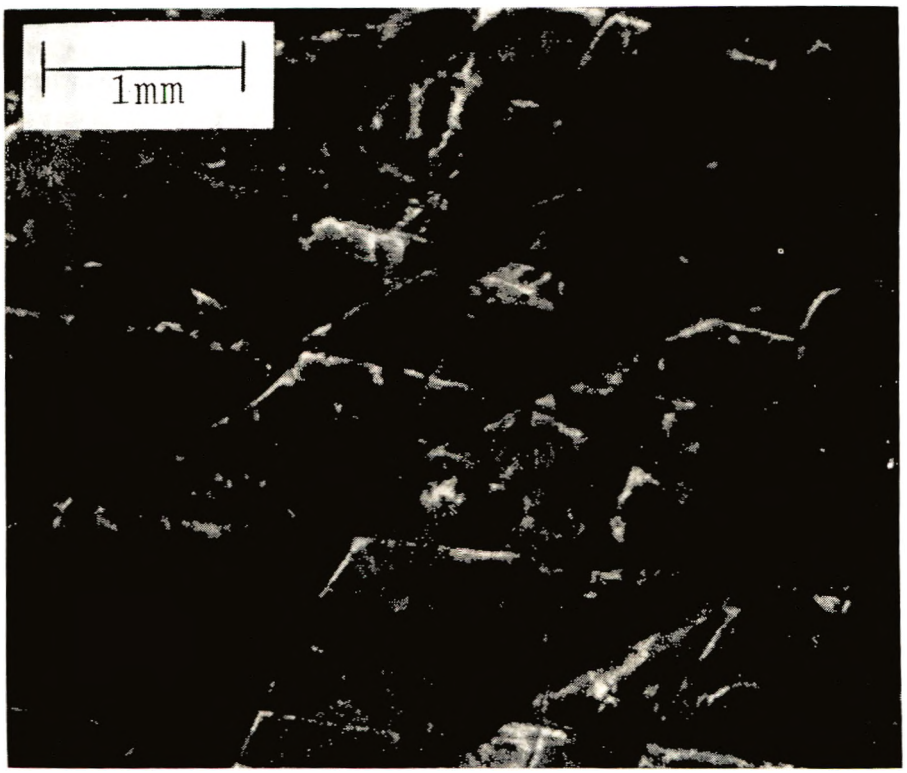

Figure 2. Optical photomicrograph of skin having dryness rating of 3

distribution of scale and cracking. Gross signs of dryness, which are visible to the naked eye and the tactile evaluation of roughness are taken into account.

II. *Rating System*

A rating system has been developed in order to obtain a numerical expression of relative dryness. The definitions of ratings from 0 to 5 are depicted in Table I. The +3 rating is a reference point, which relates the microscopic numerical rating system with the degree of dryness just noticeable to the subject.

At low magnification (30 X), the skin surface of most subjects consists of diamond-shaped plateaus outlined by furrows or sulci (Fig. 1). Unless the skin is dry, both plateaus and sulci are smooth in appearance. As the surface dries, scales appear on both plateaus and sulci (Fig. 2). Cracking occurs at the bottom of the sulci with advanced dryness (Figs. 3 and 4). Relatively few individuals (about 5 per cent), have skin in which the plateaus have a "cobblestone" appearance. As a rule, this type of individual develops smaller scales than does the average individual, and these occur primarily on plateaus.

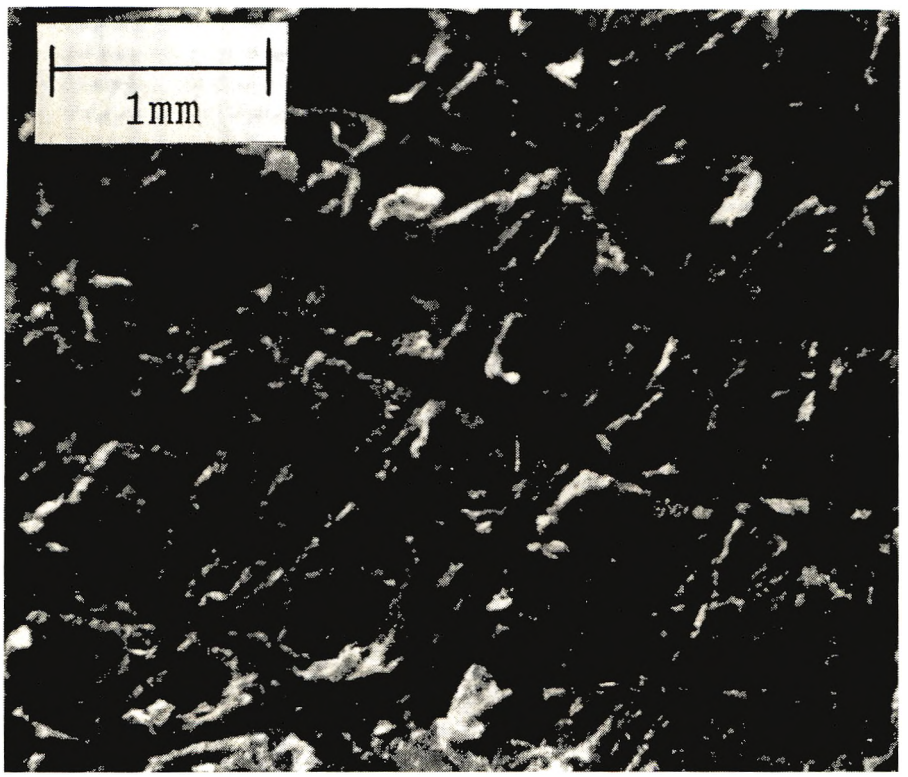

Figure 3. Optical photomicrograph of very dry skin having dryness rating of 5

III. *Test Procedure*

Both of each individual's hands are rated for initial dryness on the morning of the first test day using the scale described previously. Both hands are washed with unscented, 80:20 tallow cocoa hand soap 5 times per day at approximately hourly intervals for 4 days. Hands are washed for 30 sec, so that the backs of both hands are equally exposed to lather. They are thoroughly rinsed with tepid tap water and patted dry, except for the backs of both hands, which are allowed to air dry. Following each of the first 4 washings, the test material is applied to the back of one hand using the first 3 fingers of the opposite hand with a circular motion; the other hand serves as the untreated control.

Written instructions are given to each panelist at the start of the test. Panelists are cautioned not to transfer test material to the back of the untreated hand and to avoid rubbing or scratching either hand during the test period. The product is applied each day only after the first 4 washings. The fifth washing is necessary to remove the test material, which might interfere with

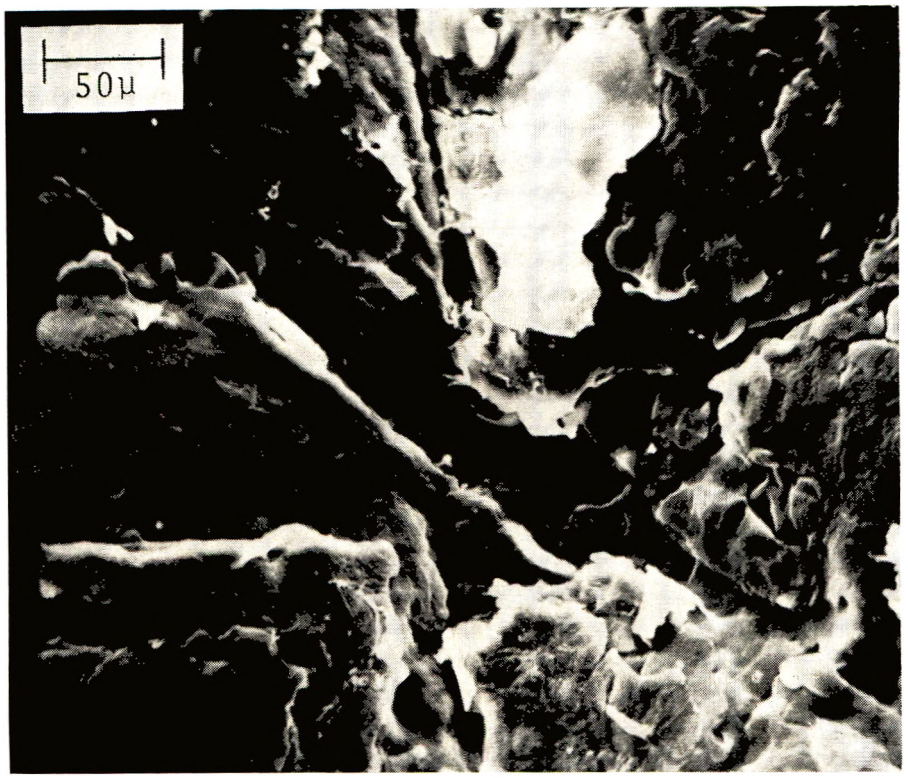

Figure 4. Scanning electron micrograph of very dry skin. Note cracking in sulci

stereomicroscopic observation. About an hour is required for the skin to equilibriate to its original moisture content after washing. Therefore, subjects are instructed to return for evaluation each day, 1 to 1½ hours after the final washing.

Thoroughness of washing can be checked by means of the dryness rating of the untreated hand. For panels of 5, theoretical maximum dryness per panel is 100 (5 panelists with 4 observations per panelist, each having a daily rating of 5). Aggregate dryness ratings of 70 to 80 are routinely obtained on such panels.

It has been our experience that frequent reminders to panelists of the importance of following the above regimen produce positive responses. Panelists are instructed to avoid the use of hand-care products during the test period and to wash their hands only at scheduled times before observation each day. Following this, they are permitted to follow their usual routine (washing dishes, etc.), except for the use of hand care products, until the resumption of testing the next day.

To qualify as panelists, volunteers must have a propensity for dry skin at colder times of the year and develop dry skin (5 rating) on both hands after four days of the above regimen, without the use of test material. Suitable panelists usually develop maximum ratings on both hands by the third test day.

IV. *Elimination of Bias*

Volunteers who pass the preliminary washing test are assigned a number. Numbers are drawn at random from the pool of acceptable panelists, until the required number of panels is completed. When panels of five are run, 6 panelists are chosen, and the sixth panelist serves as a supernumerary, and his or her values are used only if one of the first 5 panelists is absent at any time during the test period. Determination of panel size will be discussed later.

The choice of hand to be treated is randomized and balanced. Panelists are rested for at least 1 week between tests to avoid starting the test with hands that differ widely in dryness. The observers are unaware of what materials are being tested and which hand is treated. Each test day, the panelists report to a coordinator in a separate room who gives them a slip of paper identifying the hand to be examined. This is carried to the observer who examines the hand and writes its rating on the slip, which the panelist returns to the coordinator. The sequence of hand examination is also randomized. The coordinator distributes test material and an instruction-comments form on the first day. Panelists are instructed not to discuss the test with the observer.

V. *Determination of Numerical Moisturizing Rating Results Obtained Using* ***5-Member Panels***

Treated and untreated hand values are summed for all members of the panel. The aggregate value of treated hands is subtracted from the total for untreated hands to obtain the "difference" due to treatment. The greater the total difference is, in a positive sense, the greater is the moisturizing efficacy of the test material. Samples that obtain difference ratings above 40 after 4 days, with 5-member panels, are considered to be excellent moisturizers. Differences of 30-to-40 are rated as good. Distilled water has no effect on this test, as one would expect, obtaining difference ratings of approximately 0. Difference ratings of some typical cosmetic ingredients obtained with 5-member panels are shown in Table II.

Of interest is the moisturization advantage of glycerine over propylene glycol, and sorbitol. All are humectants and are widely used in products because of their humectant properties. Mineral oil and petrolatum perform well, as one might predict, from their known occlusive nature. Silicone fluid obtained a relatively poor rating; this might be anticipated from the relatively low water

Table II
Effectiveness of Some Commonly Used Cosmetic Ingredients

Ingredients Tested	Stereomicroscope Ratings		
	Treated Hand	Untreated Hand	Difference (Untreated-Treated)
Petrolatum	18	72	+54
Mineral oil—light	24	73	+49
Vegetable oil triglyceride	42	76	+34
Glycerine (25 per cent in H_2O)	34	68	+34
Propylene glycol (25 per cent in H_2O)	71	70	− 1
Sorbitol (25 per cent in H_2O)	73	87	+14
Silicone fluid (dimethyl polysiloxane)	58	78	+20

diffusion resistance of silicones as a class, as was reported by O'Neill and Goddard (17).

VI. *Statistical Approach to Testing*

The use of small panels (5 members plus a supernumery) provides an estimate of relative moisturizing efficacy, that is useful as an aid to formulation and also, in the evaluation of potential moisturizing ingredients. In order to discriminate, at an acceptable level of confidence, between products whose scores are not markedly different, more rigorous test conditions must be used.

The following experiments were performed to establish test requirements for obtaining statistically valid data. An estimate of reproducibility was obtained by testing the same product with 4 simultaneous panels consisting of 5 subjects each. The observer was unaware that the panels were duplicates. Results are shown in Table III. From the aggregate scores obtained, we computed a standard deviation of 6.8 points among the panels.

Since we are interested in refining the detection of difference to as little as 10 or 15 points, the number of replications of 5-member panels required to detect such differences was determined for the 95 per cent confidence level. It was found that 5 replications were necessary to detect a difference of 10 points and that 2 were required to detect a 15-point difference. A double-blind experiment was then performed in which the following conditions were imposed: two observers in separate rooms rated individual hands with a screen between themselves and the subjects (Fig. 5).

Twelve-member panels were used; panelist selection, choice of hand to be treated, and the sequence of hand examination were randomized. On one occasion, during the four-day test, both observers examined each of the panelist's hands twice. In this manner, it was possible to determine the ability of observers to repeat themselves and to compare one observer's values with the other's. Under these conditions, it was found that observer-to-observer error

Table III
Five-Membered Panels—Reproducibility

Panel	Dryness Rating										
	DAY 1		DAY 2		DAY 3		DAY 4		Weekly Total		Difference
	T[a]	U[b]	T	U	T	U	T	U	T	U	(U-T)
#1 J.C.	2	2	1	4	3	5	1	4			
R.N.	4	3	4	5	4	5	5	5			
R.C.	4	4	4	5	4	5	4	5			
T.V.	5	3	0	3	0	4	1	3			
B.H.	1	2	2	5	2	5	0	5			
Daily total	16	14	11	22	13	24	11	22	51	82	+31
#2 H.Z.	1	4	1	5	2	5	0	5			
C.G.	1	1	4	3	1	5	1	4			
J.M.	2	1	3	4	2	5	3	5			
R.A.	3	4	3	4	2	5	4	5			
W.S.	2	3	4	5	2	5	3	5			
Daily total	9	13	15	21	10	25	11	24	45	83	+38
#3 H.C.	4	3	3	5	3	5	4	5			
R.G.	3	3	4	5	2	5	0	4			
A.C.	2	3	3	5	3	5	2	5			
W.M.	1	3	2	5	2	5	2	5			
M.U.	3	4	3	5	1	5	1	5			
Daily total	13	16	15	25	11	25	9	24	48	90	+42
#4 M.Y.	3	4	3	5	1	4	1	5			
W.W.	2	0	3	5	3	5	1	5			
M.H.	2	3	1	5	0	5	1	5			
R.H.	3	2	1	3	1	4	1	2			
H.C.	1	2	0	4	0	3	0	5			
Daily total	12	11	8	22	5	21	4	22	29	76	+47

[a]T = Treated hand.
[b]U = Untreated hand: Mean difference: 39.5; Standard deviation: 6.8.

was much less than was expected. As anticipated, panelist variation made a large contribution to total error. By use of the double-blind technique, overall error was reduced to the point where differences of 10 points between panels comprised of as few as 12 people were significant at the 95 per cent level of confidence.

VII. *Computer Analysis of Data*

To facilitate organization and statistical analysis of the relatively large amount of data compiled by the double-blind testing procedure, a Fortran program was written for the IBM 1800 computer.

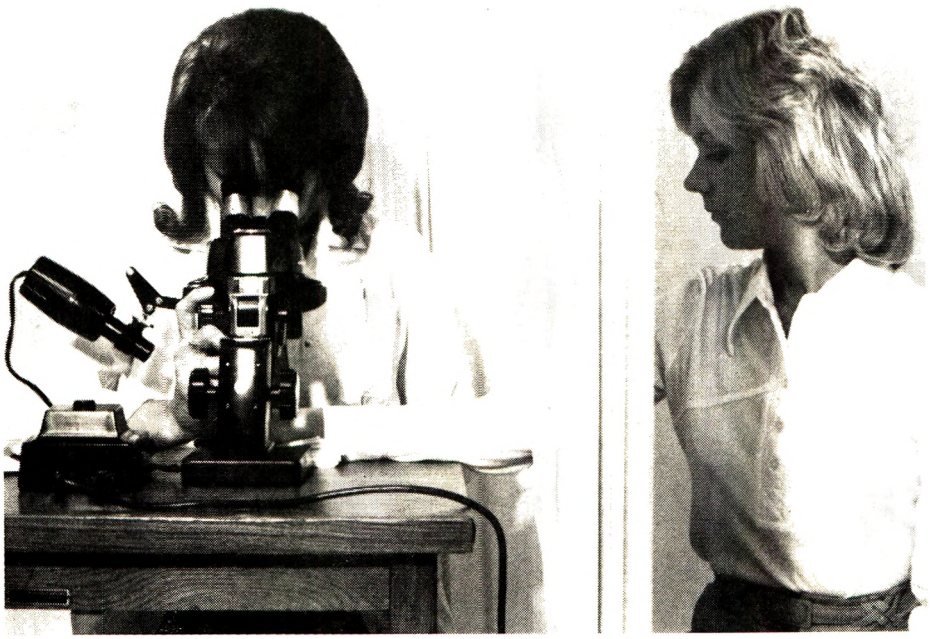

Figure 5. Stereomicroscopic evaluation of hands in double-blind study. Individual hands are rated with screen between subject and evaluator

Raw data and experimental design were encoded separately on punch cards. In this manner, total 4-day test results, an analysis of variance (ANOVA), and a table of mean values were obtained. Finally, the t-statistic was obtained, which could be evaluated using the standard student's t-table at a level corrresponding to the number of degrees of freedom contained in the error term of the ANOVA table.

VIII. *Outside Confirmation of Results*

Although replicate analysis of several test materials had indicated that the reproducibility of the stereomicroscopic method was good, the ability of others to reproduce results obtained in our laboratories was investigated. To this end, a scientist from an independent laboratory* was trained in our laboratories to evaluate hands for dryness and to administer the stereomicroscope procedure. He was also given a copy of the test protocol.

*Hill Top Research, Inc., Miamiville, Ohio.

Table IV
Comparison of Results Obtained "In-House" and by An Independent Laboratory[a]

Material Tested	Stereomicroscopic Difference Rating	
	Independent Laboratory	Avon
Propylene glycol (25 per cent aqueous)	— 7	— 1
Glycerine (25 per cent aqueous)	+31	+34
Vegetable oil triglyceride	+24	+34
Mineral oil (light)	+31	+49

[a]Hill Top Research, Inc. Miamiville, Ohio.

At the outside laboratory, 54 women with histories of dry skin were selected at the start of the study. They were placed on the usual 4-day preliminary hand washing regimen. Their instructions were identical to those used in our laboratories. At the end of the test period, they were rested for 1 week after which the 48 women with the highest scores on both hands were selected for efficacy testing using coded samples supplied by us. Results obtained in both laboratories are summarized in Table IV.

In general, agreement between the two laboratories was excellent. This was particularly true for results that were obtained with the use of propylene glycol and glycerine. Results obtained with both oils were higher in our laboratories. These results are particularly encouraging when one considers the relative inexperience of the independent laboratory with the stereomicroscope technique.

Discussion

It is generally accepted that '*in vivo*' measurement of water transmission rates is a scientifically sound procedure for measuring the ability of the stratum corneum to prevent moisture loss. Unfortunately, regardless of what device is used to measure transepidermal moisture loss, there are several problems inherent in this type of testing. Perspiration rates are severalfold greater than transepidermal loss of water. This necessitates maintaining subjects in a quiescent state at constant cool temperature and low humidity. Water content of the sample under test can also contribute substantially to control readings. Laden (18) has reported on the pitfalls associated with testing humectants such as glycerine by measurement of transepidermal moisture loss. As a result of these technical problems, the usefulness, for screening purposes, of this approach is limited to occlusive materials of low water content.

The test described here was designed to overcome these restrictions and to provide information on efficacy that otherwise would only be available, through extensive clinical testing. It is recognized that the dry skin condition, induced by repeated washing with soap and water in this procedure, may not

be physiologically identical with similar conditions resulting from exposure to the uncontrolled environment. We note, however, that at our level of observation, soap-induced dryness is not noticeably different from that observed on first examination of untreated subjects during cold, dry weather. Subjects who display signs of environmentally induced dryness and are aware of this as a seasonal cosmetic problem, can be made to develop the signs of dryness at any time of the year in this test, but they respond less readily and less intensely in warm moist weather. We have not measured this seasonal effect by direct experiment nor can we comment on the possibility of a corresponding seasonal change in responsiveness to cosmetic treatment and we must, therefore, recommend that direct comparisons of efficacy be made simultaneously.

Definitions of the terms "dry skin" and "moisturizer" have been proposed to emphasize testing parameters and foster uniformity in research on moisturization.

Acknowledgments

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References

(1) D. H. Powers and C. Fox, The effect of cosmetic emulsions on the stratum corneum, *J. Soc. Cosmet. Chem.*, **10**, 109-16 (1959).

(2) F. A. J. Thiele and K. Schulter, A new micro method for measuring the water-balance of human skin. Salt crystal method, *J. Invest. Dermatol.*, 39, 95-103 (1962).

(3) E. W. Rosenberg, H. Blank, and S. Resnick, Sweating and water loss through the skin, *J. Amer. Med. Ass.*, **179**, 809-11 (1962).

(4) H. Baker and A. M. Kligman, Measurement of transepidermal water loss by electrical hygrometry, *Arch. Dermatol.*, **96**, 441-52 (1967).

(5) D. Spruit, Measurement of water vapor loss from very small areas of forearm skin, *J. Invest. Dermatol.*, **58**, 109-13 (1972).

(6) M. M. Reiger and D. E. Deem, Skin Moisturizers. I. Methods for measuring water regain, mechanical properties, and transepidermal moisture loss of stratum corneum, *J. Soc. Cosmet. Chem.*, **25**, 239-52 (1974).

(7) K. Laden and R. Morrow, Torsional measurements on skin, *J. Soc. Cosmet. Chem.*, **21**, 417-25 (1970).

(8) A. C. Park and C. B. Baddiel, Rheology of stratum corneum. Part I. A molecular interpretation of the stress-strain curve, *J. Soc. Cosmet. Chem.*, **23**, 3-12 (1972).

(9) A. C. Park and C. B. Baddiel, Rheology of stratum corneum. Part II. A physicochemical investigation of factors influencing the water content of the corneum, *J. Soc. Cosmet. Chem.*, **23**, 13-21 (1972).

(10) M. M. Reiger and D. E. Deem, Skin Moisturizers. II. The effect of cosmetic ingredients on human stratum corneum, *J. Soc. Cosmet. Chem.*, **25**, 253-62 (1974).

(11) J. B. Shelmire, Jr., The influence of oil-in-water emulsions on the hydration of keratin, *J. Invest. Dermatol.*, **26**, 105-9 (1956).

(12) R. J. Scheuplein and L. J. Morgan, "Bound water" in keratin membranes measured by a microbalance technique, *Nature*, **214**, 456-8 (1967).

(13) J. J. Bulgin and L. J. Vinson, The use of differential thermal analysis to study the bound water in stratum corneum membranes, *Biochim. Biophys. Acta*, **136**, 551-60 (1967).

(14) K. Grice, H. Sattar, and H. Baker, Urea and retinoic acid in ichthyosis and their effect on transepidermal water loss and water holding capacity of stratum corneum, *Acta Dermato-venereol. (Stockholm)*, **53**, 114-8 (1973).

(15) S. A. M. Johnson, R. L. Kile, D. J. Kooyman, H. S. Whitehouse, and J. S. Brod, Comparison of effects of soaps and synthetic detergents on hands of housewives, *Arch. Dermatol. Syph.*, **68**, 643-50 (1953).

(16) J. M. Gibson, The evaluation of hand-care preparations, *J. Soc. Cosmet. Chem.*, **24**, 31-41 (1973).

(17) J. J. O'Neill and E. D. Goddard, Measurement of the relative permeabilities of lipoidal substances to water vapor, *J. Colloid Interface Sci.*, **25**, 57-62 (1967).

(18) K. Laden, The role of glycerol in skin hydration, *J. Soc. Cosmet. Chem.*, **13**, 455-58 (1962).

J. Soc. Cosmet. Chem., **27**, 365-376 (August 1976)

Clinical Aspects of Dry Skin

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Presented, May 1975, Annual Seminar, St. Louis, MO.

Synopsis: Adequate prevention and management of DRY SKIN problems are based on the prediction of establishing a correct diagnosis, a feat often not accomplished by patients and physicians. The incidence of DRY SKIN SYMPTOMS is increasing because of changes in the work and leisure time milieu of large portions of the population. Regulation of environmental exposure and patient education are important preventive measures. Specific methods for maintenance of STRATUM CORNEUM WATER BARRIER and BINDER CHARACTERISTICS are unknown, but many topically applied formulations, sometimes in conjunction with systemic medications, restore the skin to normal appearance clinically and rid the patient of associated symptoms. The cosmetic chemist, physician, and user of dry skin products should be aware that adverse reactions to their topical use can occur.

Clinical Aspects of Dry Skin

The tremendous magnitude of dry skin problems and associated disturbances are well known to the cosmetic industry as is evidenced by the great consumer demand for dry skin products. Let it suffice for us to say that hundreds of millions of dollars are spent annually in the United States for such products (1).

The frequency of symptomatic dry skin problems seems to be increasing faster than can be accounted for by increases in population. Increased numbers of people in the geriatric age group and man's relatively slow adaptive capacity to many changes within his environment seem to be causative. Frequency of symptomatic dry skin problems relates to such external factors as industrialization, urbanization, efficient cleansing agents, availability of hot water, news media advertisements, jet age mobility, artificial atmospheric conditions, and the anxieties produced in a complex world society.

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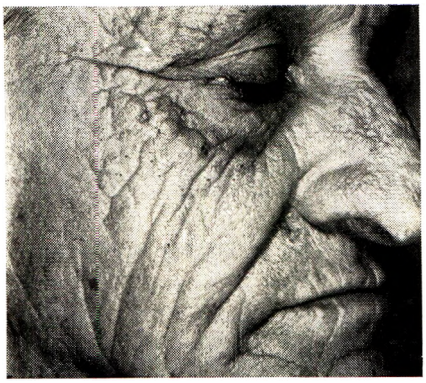

Figure 1. 69-year old person with solar damaged skin (senile elastosis, pigmentary changes, rhytidosis, and actinic keratoses) that is moist and shiny

Figure 2. Photograph of 70-year old person taken with the same ambient conditions and fixed focus camera used for Fig. 1. Note similar actinic damage, but also that skin is dry and dull in appearance

Etiology

References to dry skin can be found under many different names (2), and skin that appears dry often means different things to different observers. Neurodermatitis, fungus infections, contact dermatitis, psoriasis, seborrheic dermatitis, atopic dermatitis, pityriasis rosea, and other maculo-squamous diseases are often confused with dry skin (1, 2). Certain drugs (3) have been reported to cause dry skin, as well as many systemic conditions, although such positive relationships are sometimes not proven.

A common mistake is to equate dry skin with skin of the aged or sun damaged skin, or both. Skin exposed for many years to solar radiation may appear moist and shiny (Fig. 1) or dry and dull (Fig. 2). The lily white skin on the hips of an old person or on an infant may be very dry, but shows no evidence of actinic degeneration. Increased melanin pigment protects dark skin from the sun, but not from dehydration.

The vast majority of people with dry skin have no systemic or other specific dermatologic disease, but they lack the ability to cope successfully with the many things in the environment that adversely affect proper and continued water binding capacity of the stratum corneum. The basic reasons for this are largely unknown, but the elderly (4-7), infants and young children, and certain familial groups (4, 6) are most prone to dry skin problems.

Certain winter weather changes have been etiologically associated with dry skin since Duhring's classic article in 1874 (8), and in 1952, Gaul and Underwood's studies (4) related stratum corneum cellular destruction to wintertime changes in atmospheric dew point, barometric pressure, and wind

velocity. In 1962 Chernosky (2) found an identical clinical picture of dry skin in patients who were exposed to humid summertime weather and relatively dry refrigerated air conditioning. Clinical observations on dry skin fit with experimental studies concerning the nature of straum corneum hydraion, water binding, and water barrier properties, which have been thoroughly reviewed by Idson (9).

For over 50 years physicians have noted that soap and water (especially hot water) promote dryness of the skin, and they later noted that detergents and various solvents do the same thing (2, 4, 6, 10, 11). Numerous experimental studies have confirmed these clinical observations. Damage to water binding capacity is observed especially if the skin is exposed first to lipid solvents or detergents and then to water (12-14).

Physical damage of the skin from clothing, pressure, rubbing, and scratching have long been recognized as a causative in producing some of the clinical and histological changes in patients with dry skin.

Clinical Features

In the early stages of dry skin, only a physicochemical disruption of the nonviable stratum corneum occurs. The earliest visible change, often not appreciable to the untrained observer, consists of a dull, greyish-white color with increased prominence of topographical lines that, upon close inspection, look like an irregular mosaic (Fig. 3). Compare this change with normal appearing skin in the same anatomic area (Fig. 4). As changes in hydration of the corneum continue, the cohesiveness of the squames is partially lost, which allows a curling up of their edges and a network-like pattern of tiny

Figure 3. Earliest visible changes of dry skin (see text)

Figure 4. Normal skin of same anatomic location shown in Fig. 3

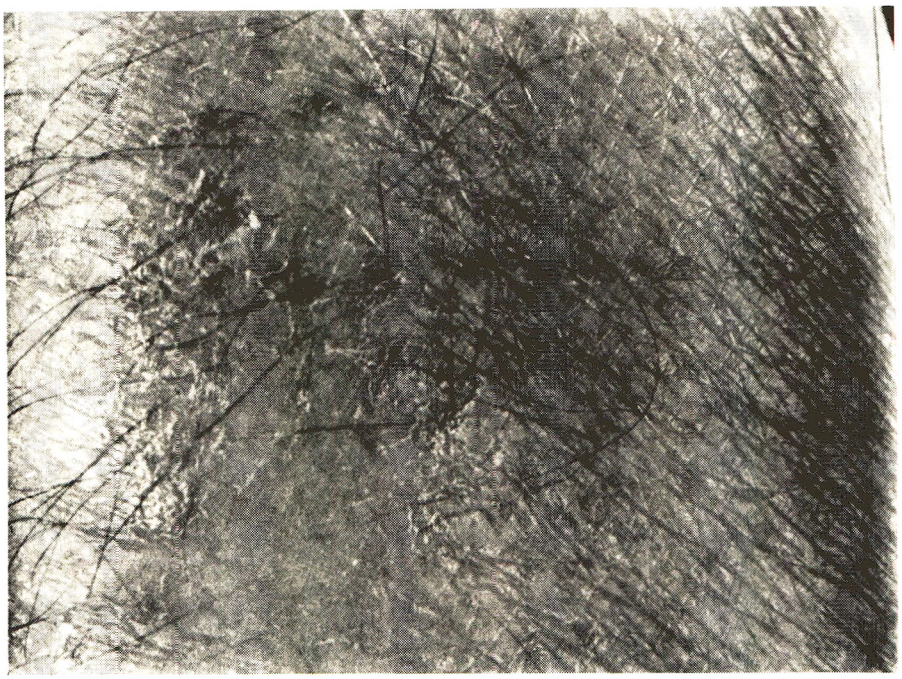

Figure 5. Dry skin showing loosening of edges of surface squames and irregular pattern of chaps

chaps (slits) in the skin surface (Fig. 5). Sometimes this change is more marked at follicular orifices (Fig. 6). At first, the chaps involve only the stratum corneum, but they may progress deeper and become fissures that extend into the malpighian layer and even the dermis, thus causing biologic damage and stimulating an inflammatory response, which is clinically observed as erythema, edema, exudation, crusting, and occasionally, purpura (15). Loosening of entire squames from the surface results in shedding of dry scales. The skin surface looks and feels rough, and the patient may describe a feeling of loss of pliability when the skin is moved or stretched. Pruritus and a stinging sensation may be present, and various types of trauma from rubbing, scratching, and clothing friction aggravate these symptoms and produce more surface damage, erythema, and edema, but rarely any vesiculation. A chronic lichenified dermatitis with pigmentary changes may ensue if the condition persists (Fig. 7). Secondary bacterial infection may also occur.

Distinct plaques of eczema may appear, sometimes with central clearing (Fig. 8), which resemble dermatophytosis. Some observers believe that trauma causes these patches to develop, but their nummular and avoid ap-

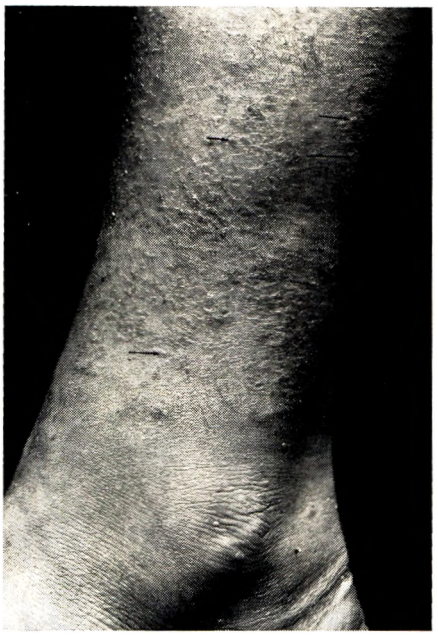

Figure 6. Dry skin on leg showing accentuation of change at some of follicular orifices (arrows)

pearance and distribution pattern makes this theory difficult to accept. Spottiness of many skin diseases is an enigma. Whimster (16) has postulated the presence of a central nervous system controlled organized mosaic in human skin, which remains invisible until pathology occurs. Application of his theory has been suggested as a possibility in one pigmentary disorder (17).

Diagnosis of the dry skin syndrome is aided by recognition of its rather characteristic distribution pattern (Figs. 9, 10). Lateral surfaces of the arms, forearms, dorsa of hands, iliac and gluteal areas, lateral and anterior thighs, and the legs are most commonly involved. The lower portion of the face is often involved if the skin is artificially wetted because of licking or the drooling of saliva from the corners of the mouth, a problem often associated with decreased vertical facial dimension (18) (Fig. 11).

Other reasons for the distribution shown in Figs. 9 and 10 include greater exposure to adverse atmospheric conditions, damage from soap, detergents, and solvents, pressure or sliding trauma from daily activities and clothing, easy accessibility to self-inflicted injury (rubbing, scratching), less sweating (and greater loss of surface sweat to atmosphere), and possibly to lowered sebum production. If etiologic factors persist, dry skin changes can spread to

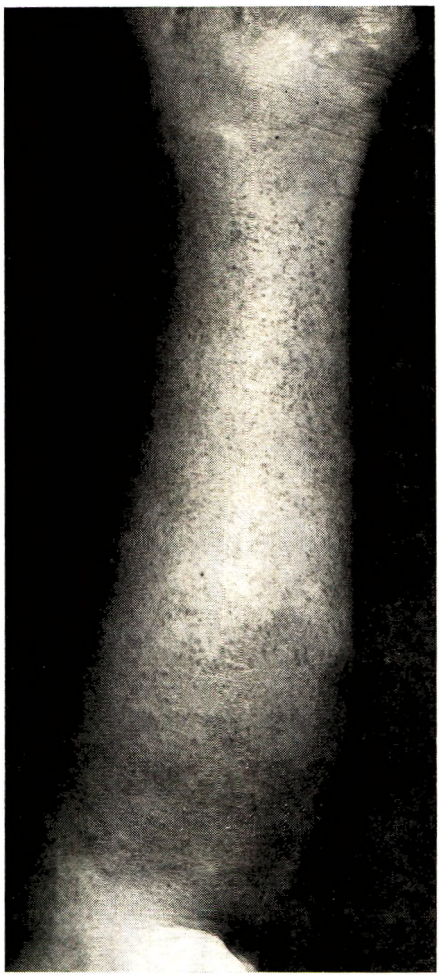

Figure 7. Chronic lichenified skin caused from persistant hydration changes and associated symptoms.

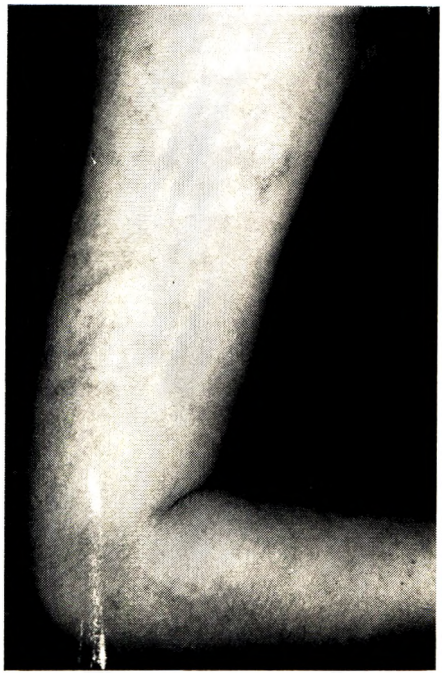

Figure 8. Dryskin of arm showing well delineated plaques of dermatitis

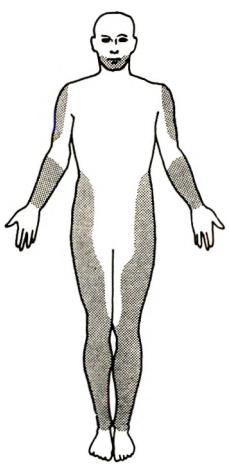

Figure 9. Anterior view showing most common distribution pattern of dry skin changes

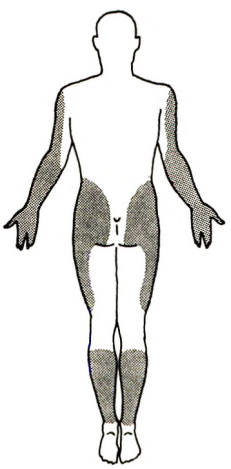

Figure 10. Posterior view of distribution pattern of dry skin changes

Figure 11. Chapped skin with fissuring at oral commissures (perlèche) and on chin.

other areas, but ordinarily do not involve flexural or intertriginous areas of skin supplied with large amounts of sebum.

Prevention and Management

Total prevention of abnormally dry skin is not feasible in large portions of the population. Some groups are prone to dry skin problems because of age or genetic predisposition, or both. But every person's skin can develop dry skin signs and symptoms provided they are subjected to sufficient environmental insults.

Environmental Control and Protective Measures: Clinical and experimental observations which were alluded to previously indicate the effects of ambient conditions on skin dehydration and hydration. A patient subjected to windy dry weather conditions, at high or low temperatures, should be instructed to cover his skin with loose fitting clothing so as to be better provided with a more isolated, private cutaneous atmosphere. The burnoose of the Bedouin is a more protective piece of clothing than are the shorts British soldiers wear in the desert.

The jet age makes more people nomadic, and quick moves from humid climates to dry ones increase one's proneness to dry skin problems. Chapping

of skin has been a problem associated with soldiers who return from the tropics to California (19).

According to temperature, humidity, and air motion thermoequivalent charts published by air conditioning engineers (20), relative humidities below 70 per cent at room temperature have no appreciable effect on human comfort related to subjective warmth or cold, but such studies do not relate to dry skin production and associated symptoms. Winter weather air conditioning systems should provide adequate moisture to the air. Ideally, the low relative humidity of summertime refrigerated air conditioning should be raised, but engineering problems and expense apparently prevent this. Air conditioning systems, winter and summer, should be built according to published specifications in order to prevent a feeling of draft. In many instances, this is often not the case, (e.g. as in automobiles and window units).

Patients with a proneness to dry skin should decrease their exposure to soaps, detergents, and lipid solvents. Hot water exposures are more harmful than cold water ones. A single long exposure seems to be less damaging than multiple short exposures. Protective gloves with sweat absorbing liners, frequently changed, are useful. Mechanical irritation from clothing (especially wool), household activities, and job-related duties should be decreased and, of course, the patient should be encouraged to inhibit self-inflicted damage from rubbing and scratching.

Topical Preparations: The pharmaceutical and cosmetic industries and extemporaneous prescription writing physicians have produced hundreds of products for topical use to prevent and treat dry skin. Plainly, this indicates that we do not as yet have the ideal preparation.

Many of the popularly used water-dispersible bath oils and oil-in-water emulsion lotions and creams give relief by coating the surface with a film that makes the skin look and feel more normal. They are easy to apply and are cosmetically acceptable. Their major mode of action probably relates to providing more cohesion for the unattached edges of squames and leaving an oily surface with a lower coefficient of friction, but some products contain sufficient amounts of materials with a significant water vapor loss resistance to trap some moisture within the stratum corneum. Their effectiveness is usually of short duration and, frequently, many applications per day are required.

Other types of products are capable of absorbing water and temporarily holding this additional moisture on the skin surface. For generations, mothers have taught daughters about the beneficial effect of mixtures of glycerin and rose water on dry hands, and, for many years, some dermatologists have prescribed mixtures of glycerin, peppermint water, and ethanol (21). Materials in the stratum corneum, referred to as the natural moisturizing factor (22) have a combined hydroscopic ability that closely resembles that of glycerin (23). Propylene glycol and certain carbowax mixtures have similar

water absorbing powers, and Goldsmith and Baden (24) have used this power to treat ichthyosis. Unfortunately, the effectiveness of this group of products on dry skin is of short duration.

More prolonged relief of dry skin signs and symptoms can be obtained by applying materials with a high water vapor loss resistance that prevent water from sweat and transepidermal transport from leaving the surface. Certain water-in-oil emulsions and lipid materials of high viscosity provide this protection. For example, petrolatum has a water vapor loss resistance 17 times that of liquid paraffin and 170 times that of olive oil (25). But the cosmetic industry realizes the difficulty of promoting materials resembling petrolatum because of the cosmetic unacceptability related to a greasy feeling, stickiness, and interference with surface skin cooling. Their use is frequently limited to the more severe cases of dry skin.

Sodium chloride, in various bases, and even set bathing, have been advocated for treatment of ichthyosis, but I know of no controlled study that shows a beneficial effect in ordinary dry skin problems.

Urea has been advocated for various skin problems, and, in 1957 Kligman (26) reviewed its usefulness in dermatologic therapy. Urea causes an increase of water uptake by stratum corneum (27); has an antipruritic effect (28); increases percutaneous absorption (29) and clinical effetiveness (30) of hydrocortisone; and has been shown to be useful in chronic eczemas (31) and various types of dryskin diseases (32). Some studies indicate its usefulness for ichthyosis (27, 33, 34), and uncontrolled studies suggest its benefit for dry skin (35, 37). But I know of no published double blind study showing that creams that contain urea are superior to creams without it, although such studies are in progress. One double blind study on dry skin concluded that no statistical differences existed between creams that contain urea and aqueous creams (38).

Topical and systemic pharmaceutical preparations are sometimes required to treat severe dry skin and associated complications, but details of their indications are not germaine to this presentation.

Adverse Reactions From Dry Skin Products

It has been observed that adverse reactions sometimes occur when preparations are used on dry skin. Unfortunately, some manufacturers ignore this problem, when they state in their promotional literature, that no contraindications, precautions, or adverse reactions exist in their products.

Allergic contact dermatitis may result from preservatives, perfumes, excipients, solubilizers, emulsifiers, lubricants, and other constituents. Symptomatic primary irritant type contact dermatitis has been observed (39). Nonspecific discomforts include a warmth sensation, greasy or slimy feeling, and problems with contamination of clothing and papers. Disturbances in ecology

of the cutaneous microflora may result from the occlusiveness of products. Common problems such as acne, impetigo, and heat rashes may be made worse. Lipid pneumonia (40), eye irritation (41), and urethritis have been caused by dry skin products. Fortunately, unfavorable reactions to dry skin preparations are not commonly observed.

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References

(1) M. E. Chernosky, Dry skin and its consequences, *J. Amer. Med. Women's Ass.*, **4**, 133-45 (1972).
(2) M. E. Chernosky, Pruritic skin disease and summer air conditioning, *J. Amer. Med. Ass.*, **179**, 1005-10 (1962).
(3) R. L. Baer and B. B. Levine, Adverse cutaneous reactions to drugs, in *Dermatology in General Medicine*, T. B. Fitzpatrick, et al., Eds., McGraw-Hill, 1971, p. 1298.
(4) E. Gaul and G. B. Underwood, New York, Relation of dew point and barometric pressure to chapping of normal skin, *J. Invest. Dermatol.*, **19**, 9-19 (1952).
(5) F. H. Stern, Pruritus hiemalis, A frequent disturbance among the elderly, *Psychosomatics*, **7**, 248-50 (1966).
(6) I. B. Sneddon, Winter ailments of the skin, *Practitioner*, **201**, 886-91 (1968).
(7) A. Rook, D. S. Wilkinson, F. J. Ebling, eds., *Textbook of Dermatology*, F. A. Davis Co., Philadelphia, 1968.
(8) L. A. Duhring, Pruritus hiemalis, An undescribed form of pruritus, *Phila. Med. Times*, **4**, 25-30 (1874).
(9) B. Idson, Water and the skin, *J. Soc. Cosmet. Chem.*, **24**, 197-212 (1973),
(10) W. T. Corlett and H. N. Cole, A recurrent disease of the skin associated with high winds and cold weather for which the name dermatitis hiemalis has been proposed, *Amer. J. Med. Sci.*, **143**, 868-85 (1912).
(11) H. D. Niles, Winter eczema of the arms, *Arch. Dermatol., Syph.*, **39**, 474-78, (1939).
(12) I. H. Blank, Further observations on factors which influence the water content of the stratum corneum, *J. Invest. Dermatol.*, 21, 259-71 (1953).
(13) I. H. Blank and E. B. Shappirio, The water content of the stratum corneum, effect of previous contact with aqueous solutions of soaps and detergents, *J. Invest Dermatol.*, **25**, 391-401 (1955).
(14) J. D. Middleton, The mechanism of water binding in stratum corneum, *Brit. J. Dermatol.*, **80**, 437-50 (1968).
(15) R. M. Caplan, Superficial hemorrhagic fissures of the skin, *Arch. Dermatol.*, **101**, 422-51 (1970).
(16) I. W. Whimster, An experimental approach to the problem of spottiness, *Brit J. Dermatol.*, **77**, 397-420(1965).
(17) M. E. Chernosky, *et al.*, Famailial progressive hyperpigmentation, *Arch. Dermatol.*, **103**, 581-98 (1971).
(18) M. E. Chernosky, Relationship between vertical facial dimension and perlèche, *Arch. Dermatol.*, **93**, 332-37, (1966).
(19) H. V. Allington, Chapping of the skin on returning to a cooler climate, *Arch Dermmatol. Syph.*, 62, 141-42 (1950).
(20) ASHRAE Handbook of Fundamentals, American Society of Heating, Refrigeration and Air Conditioning Engineers, New York City, 1967, Pp. 111-26.
(21) Roy L. Kile, *Another Simple Dry Skin Lotion, The Schoch Letter*, Ed., A. C. Schoch, Dallas, Tex., 1974.
(22) O. K. Jacobi, About the mechanism of moisture regulation in the horny layer of the skin, *Proc. Sci. Sect. Toilet Goods Assoc.*, 31, 22 (1959).
(23) H. W. Spier and E Schwarz, *Chemie der Hornschicht* in *Proc. XII Int. Cong. Dermatol., Excepta Med. Found.*, **1**, 389 (1962).

(24) L. A. Goldsmith and H. P. Baden, Propylene glycol With occlusion for treatment of ichthyosis, *J. Amer. Med.. Ass.*, **220**, 579-80 (1972).
(25) D. Spruit, The interference of some substances with the water vapour loss of human skin, *Dermatologica*, **142**, 89-92 (1971).
(26) A. M. Kligman, Deruatologic uses of urea, *Acta Dercato-Venereol.*, 37, 155-59, (1957).
(27) G. Swanbeck, A new treatment of ichthyosis and other hyperkeratotic conditions, *Acta Demato-Venereol.*, **48**, 123-27 (1968).
(28) G. Swanbeck and G. Rajka, Antipruritic effect of urea solutions, *Acta Dermato-Venereol.* (Stockholm), **50**, 225-27 (1970).
(29) R. J. Feldmann and H. I. Maibach, Percutaneous penetration of hydrocortisone with urea, *Arch. Dermatol.*, **109**, 56-9 (1974).
(30) T. C. Hindson, Urea in the topical treatment of atopic eczema, *Arch. Dematol.*, **104**, 284-5 (1971).
(31) H. Rattner, Use of urea in hand creams, *Arch. Dermatol. Syph.*, **48**, 47-9 (1943).
(32) W. D. Stewart, *et al.*, Urea cream *Cutis*, **5**, 1241-42 (1969).
(33) F. M. Pope, *et al.*, Out-patient treatment of ichthyosis: A double-blind trial of ointments, *Brit. J. Dermatol.*, **86**, 291-6 (1972).
(34) K. Grice, *et al.*, Urea and retinoic acid in ichthyosis and their effect on transepidermal water loss and water holding capacity of stratum corneum, *Acta Dermato-Vener.* (Stockholm), **53**, 114-8 (1973).
(35) D. P. Nash, Urea cream for dry skin, *J. Amer. Podiat. Ass.*, **61**, 382-84 (1971).
(36) L. DeVleeschouwer and J. De Bersaques, Urea as a topical agent in dermatology, *Arch. Belges Dermatol.*, **27**, 225-27 (1971).
(37) R. Blake, Treatment trial for dry skin, *Current Podiatry*, 13-14 (Oct. 1972).
(38) A. T. K. Baillie, *et al.*, Carbamide in hyperkeratosis, *Practitioner*, **210**, 294-6 (1973).
(39) M. E. Chernosky, Reactions to bath preparations, emollients and other dry skin preparations, *Symp. Cosmet. Reactions*, American Academy of Dermatology, Chicago, Dec. 1973.
(40) S. A. Hurvitz, Lipid pneumonia, A new etiology, *J. Thorac. Cardiov. Surg.*, 63, 551-2 (1972).
(41) M. S. Norn, Eyelid ointment penetrating into conjunctival sac, *Acta Ophthalmol.*, **50**, 206-9 (1972).

Book Reviews

CONTACT DERMATITIS, Edited by Dr. C. D. Calnan (London). Munksgaard, Copenhagen K, Denmark, 1975. $38.20 per volume of 6 issues per year (in English).

As stated by the editor, the aim and scope of this new journal are designed as a review of world literature for clinicians, who are interested in various aspects of environmental dermatitis. This includes both allergic and irritant types of contact dermatitis, occupational dermatitis, and consumers' dermatitis from such products as cosmetics and toiletries. It is in this latter regard that *Contact Dermatitis* becomes a necessary adjunct to the American dermatological journals.

The first issue of Volume 1 (which was published in January 1975) contained 8 articles, 5 of which were germane to the cosmetic and pharmaceutical industry, namely-"Contact Dermatitis from Ethanol;" "Dermatologic Effects of Cosmetics;" "Photodermatitis;" "Chlorocresol Sensitivity;" "Chamber Test Versus Patch Test for Epicutaneous Testing;" and one article for the fragrance industry—"Aroma Chemicals."

The increasing tempo of governmental and consumer pressures, with regard to product safety and reporting of adverse reactions, makes this new journal especially valuable in providing a world-wide review of contact dermatitis in all its forms. When it is used in conjunction with A. A. Fisher's book, which is also entitled *Contact Dermatitis* (2nd ed., Lea and Febiger, Philadelphia, 1973), this journal provides a continually up-dated review of the subject. As the editor so aptly phrases it—"We live in one world in which discoveries, developments, and problems in one continent are likely to be relevant and important to doctors and scientists in every other continent."

Its Editor-in-Chief is the eminent British dermatologist, Dr. C. D. Calnan, supported with an editorial advisory board of 29 dermatologists from 13 countries.

Contact Dermatitis is highly recommended to those engaged in cosmetic, toiletries, and topical pharmaceutical product development, as well as pharmacologists engaged in product safety testing.—GABRIEL BARNET—Helena Rubinstein.

AUTHORS PLEASE NOTE:

Page charges for contributed articles published in The Journal of the Society of Cosmetic Chemists will be $25 per printed page, effective with the February 1977 issue. Page charge costs should be considered as a part of necessary research expense. While acceptance of manuscripts for publication is not contingent upon payment of page charges, it is anticipated that sponsors of research will assume some of the costs of publication.

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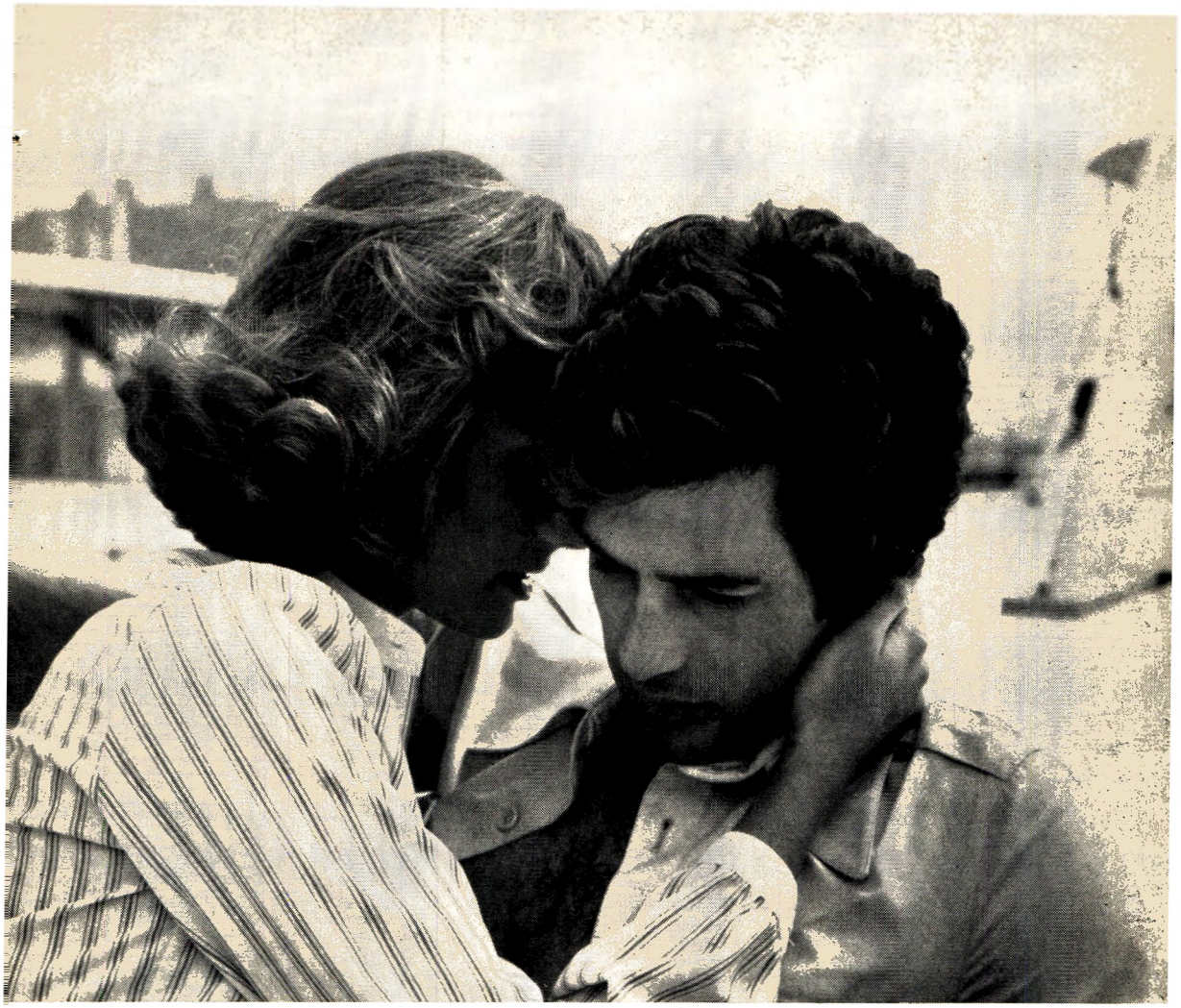

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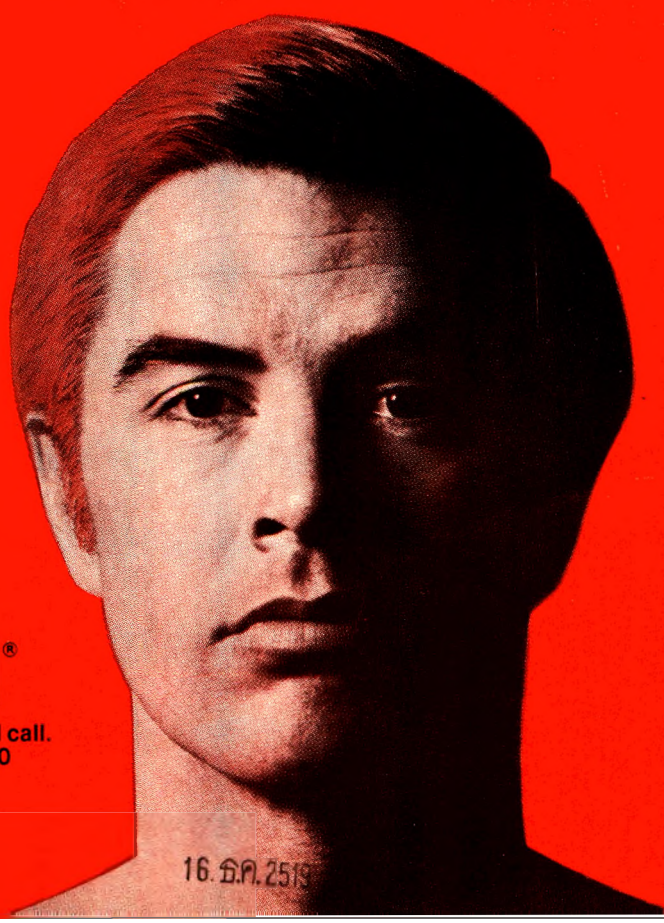

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