VOL XVIII No 11 14 OCTOBER 1967

Journal of the Society of Cosmetic Chemists

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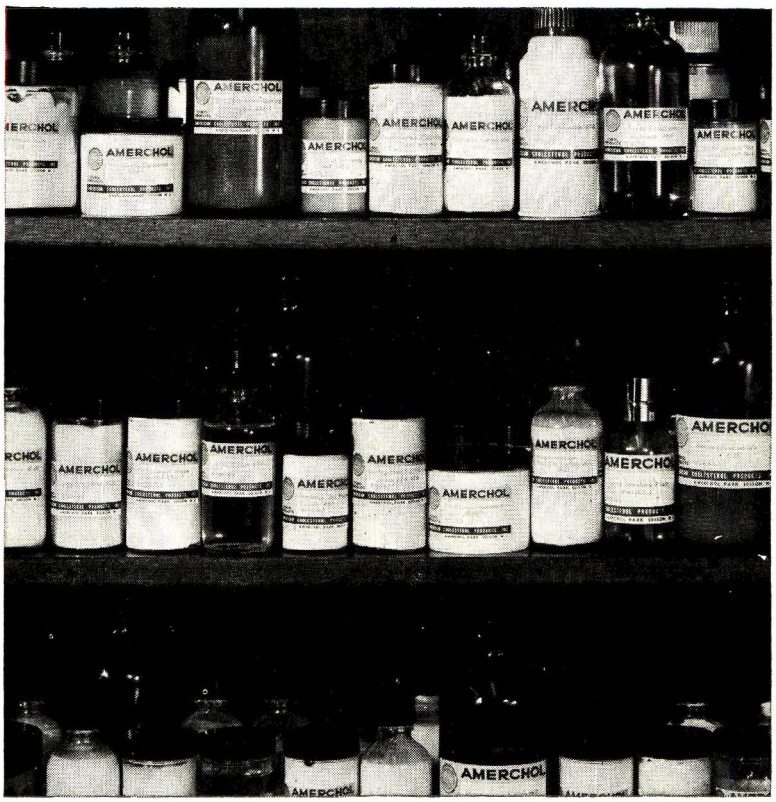

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The following synopses can be cut out and mounted on 5″ × 3″ index cards for reference without mutilating the pages of the Journal.

The behaviour of hair at low pH values: M. M. BREUER and D. M. PRICHARD.
Journal of the Society of Cosmetic Chemists **18** 643-650 (1967)

Synopsis—The effects of exposure to acidic solutions (pH < 2) on hair were investigated. It was found that considerable changes occur in the titration curve, the mechanical properties, and the reactivity of the disulphide bonds as a consequence of soaking hair in solutions having pH values less than 2. The experimental results were interpreted by assuming that a dissociation of disulphide bonds occurs in the presence of acid.

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The potential irritancy to the rabbit eye mucosa of commercially available cream shampoos: R. E. DAVIES and K. H. HARPER.
Journal of the Society of Cosmetic Chemists **18** 663-679 (1967)

Synopsis—A study has been made of the irritancy to the rabbit eye mucosa of five commercially available cream shampoos, employing four different screening procedures. It is concluded that all five shampoos are "irritants" to the rabbit eye mucosa. Three show severely irritant properties and one other clearly falls under suspicion in this respect. Results obtained by the different methods are discussed.

Contact dermatitis from cosmetics: E. CRONIN.
Journal of the Society of Cosmetic Chemists **18** 681-691 (1967)

Synopsis—Allergic reactions to cosmetics are described and the difficulties in technique and interpretation of patch tests are discussed. Lipstick, nail varnish and hair dyes are the most common sensitizers but sensitivity to lanolin also occurs. An unusual urticarial reaction to hair bleach and a phototoxic effect of perfume are described.

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J. Soc. Cosmetic Chemists **18** 643-650 (1967)

The behaviour of hair at low pH values

M. M. BREUER* and D. M. PRICHARD*†

Synopsis—The effects of exposure to acidic solutions (pH<2) on hair were investigated. It was found that considerable changes occur in the titration curve, the mechanical properties, and the reactivity of the disulphide bonds as a consequence of soaking hair in solutions having pH values less than 2. The experimental results were interpreted by assuming that a dissociation of disulphide bonds occurs in the presence of acid.

Introduction

It was previously reported that human hair undergoes irreversible structural changes when exposed to solutions of pH less than 2 (1). In particular the acid titration curve, the water regain and the value of the 30% index of hair was found to be effected by exposure to acid. In the present communication we intend to report further experimental data on the behaviour of human hair at low pH values, and suggest a molecular mechanism which accounts for these phenomena.

Experimental

Materials

Virgin hair was used throughout the experiments. The hair samples were first washed with hot distilled water to remove foreign matter; and then Soxhlet-extracted with diethylether for 24 hr. Subsequently the hair was soaked in distilled water for 4 days, the water being changed twice

*Unilever Research Laboratory, Isleworth, Middx.
†Work carried out as part of DMP industrial training programme for B.Sc. of University of Bath.

a day. Afterwards it was dried in vacuo over phosphorus pentoxide, and finally chopped to pieces about 1 cm in length.

Methods

Analar grade chemicals were used in all instances except when otherwise stated. *Volucon* volumetric solutions, prepared with freshly boiled distilled water, were used for the titrations.

The tetrakis (hydroxy-methyl) phosphonium chloride (THPC) was supplied by Albright and Wilson as an 80% solution, and was used without further purification.

The Pye *Dynacap* multi-range pH meter and an E.I.L. automatic titrimeter were used with standard electrode fittings for maintaining and measuring the pH.

A Unicam SP500 spectrophotometer was used for optical density determination and an Instron tensometer (table model) was employed for the strain-stress measurements. All experiments were carried out at 25°C ($\pm$0.5°C) using thermostatically controlled water baths.

Rate of acid uptake

This was measured by the following procedure: The hair samples (2g) were introduced into a four-necked, round bottomed flask, containing 200ml 0.1M NaCl solution. The pH was adjusted to the required value and kept constant within $\pm$0.05 units by means of an automatic titrimeter. The amount of acid required to keep the pH constant was recorded as a function of time. (Acid of strength 0.05M was used).

The determinations of N-terminal amino acids were carried out using Hille's (2) method.

Cystine analysis

The Zahn-Traumann method (3) was employed.

Reduction of hair

THPC reduction was effected by treating dried hair samples with a solution of THPC (30%) for 4 hr at 35°C in a water bath (4).

The thioglycolate reduction was carried out by exposing 1g hair to 9 w/v ammonium thioglycolate solution (10ml) at pH 9 for 15 min. In both cases the reduced hair was washed with water, and then methylated to block all the free cystine residues using Jenkins' and Wolfram's procedure (4).

Measurement of the work to 20% stretch and hysteresis indices

The Instron tensometer was used for these experiments, suitably set to measure the work to 20% stretch index (I_{20}) of single hair fibres immersed in water. First the extension curves of single hairs were measured after 2 hr soaking in water. These hairs were then allowed to relax in water for 30 hr and soaked overnight in hydrochloric acid solutions of pH 2.0, pH 1.6 and pH 1.2 respectively. Afterwards the hairs were washed free of acid and their I_{20} again measured. The hysteresis index H_{20}, was calculated from the difference between the stretching work and the work recovered during the relaxation of the fibre.

Results

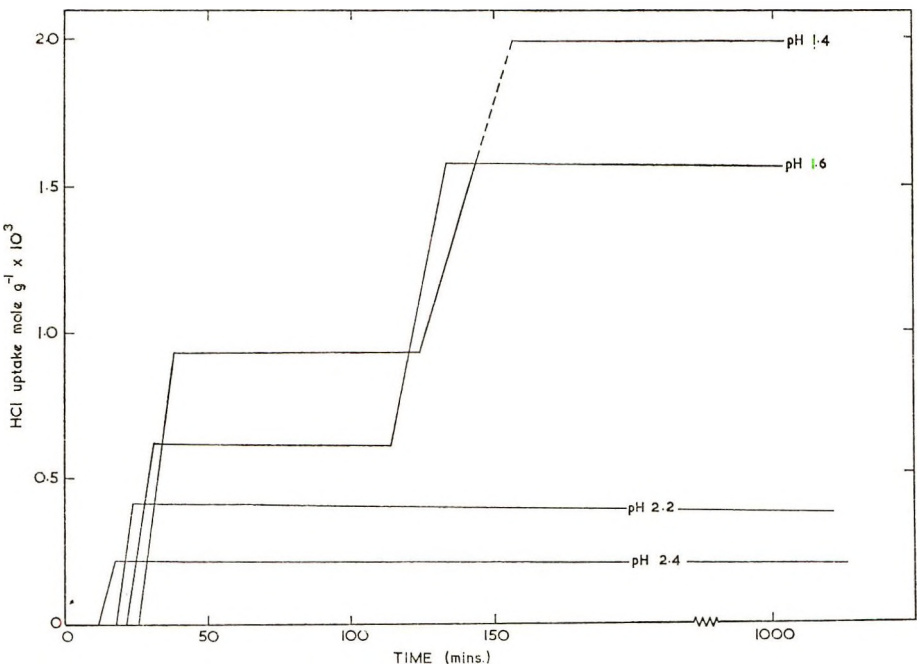

Figure 1 Curves representing the acid uptake of hair as a function of time

First we investigated the kinetics of the acid uptake using the autotitrimeter. In a three necked flask the hair was immersed in a solution of fixed pH and the acid required for maintaining the pH was measured as a function of time. The curves (*Fig. 1*) revealed that, down to approximately pH 2, the uptake occurs in a single step, reaching equilibrium in about 15

min. However, when the pH is lowered below 2, a second step occurs after about 110-120 min resulting in very much higher acid uptakes. The exact time of occurrence of the second step varied between 100-130 min after the initial exposure, possibly depending on the thickness of the hair.

In *Fig. 2* the final acid uptake (i.e. after 7 hr) is plotted against the pH. The curve of *Fig. 2* indicates clearly that in the region of pH 2 sudden

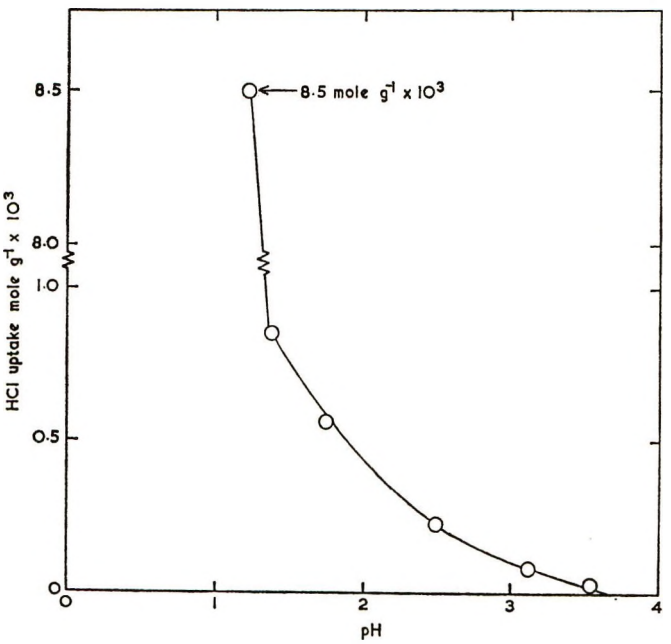

Figure 2 Acid uptake of virgin hair after seven hours' exposure to acid at 25°C

changes occur in the hair structure, causing a very large increase in acid uptake. We checked the reproducibility of the second step very carefully (*Table I*), and found that this observation could not be an artefact.

Table I Acid uptake of hair

Run	Final uptake (moles HCl/g hair)
1	8.5×10^{-3}
2	8.8×10^{-3}
3	7.9×10^{-3}

In a further series of experiments, hair samples were exposed to N/10 HCl for 12 hr at room temperature, brought back to pH 7, and washed

copiously in distilled water until the washings were neutral. The titration curves of these hair samples did not show the second step (*Fig. 3*), suggesting that the latter is due to irreversible processes taking place in the virgin hair structure.

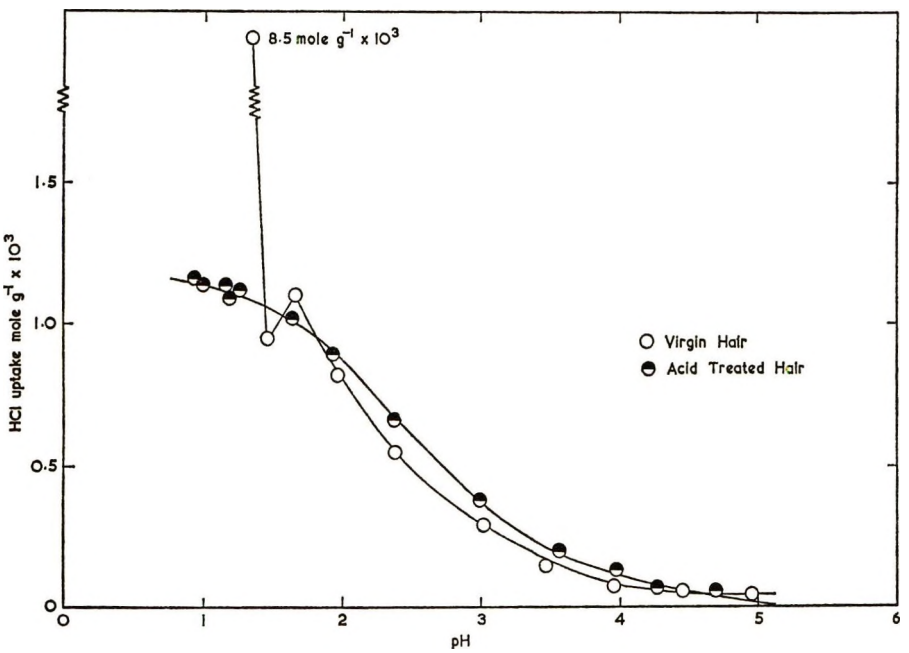

Figure 3 Acid uptake of acid treated hair (presoaked in acid and washed acid free) after seven hours' exposure to HCl at 25°C

In order to clarify whether the exposure to acid media caused hydrolysis of the main peptide chains in hair, amino acid end group analysis was carried out before and after exposure of hair to pH 1.2. The results indicated no significant degree of main chain hydrolyssis.

In another series of experiments virgin hair samples were reduced with both THPC and ammonium thioglycolate. The same procedure was also carried out with hair previously exposed to pH 1.2. All the hair samples were then methylated, hydrolysed and the fraction of intact S-S groups determined. Some typical results are given in *Table II*.

No difference (within experimental error) in the total amount of S-S content in hair was observed as a consequence of exposure to acid. The

Table II Effect of acid treatment on the reactivity of the disulphide bonds in hair

Reducing agent	% wt. total S-S	
	S-S reduction before HCl exposure	S-S reduction after HCl exposure
THPC	33.7	27.1
Thioglycolate	38.8	31.2

value of cystine content varied from sample to sample between 6.00 and 6.20%.

These results therefore indicated that at pH 1.3 an irreversible change in the hair structure occurs, making some of the disulphide bonds more stable against reduction or, alternatively, less accessible for chemical reactions.

The 20% index (i.e. the work required to stretch hair fibres to 20% extension) and the hysteresis index (i.e. the difference between the work required to stretch the fibre and the work recovered during relaxation) were determined on fibres immersed in water. The results are summarised in *Figs. 4* and *5*. (The symbols I_{20}' and H_{20}' denote the respective ratios

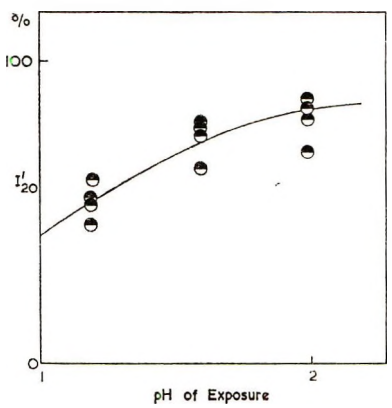

Figure 4 Plot of I_{20}' against pH

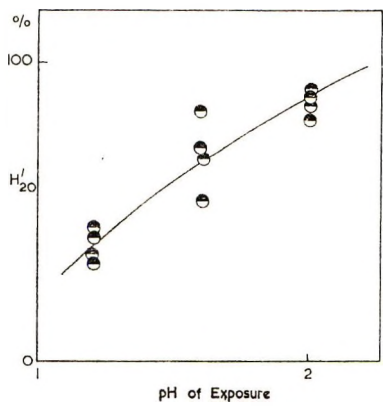

Figure 5 Plot of H_{20}' against pH

of the 20% indices and hysteresis indices of hair fibres exposed to low pHs for 12 hr to the same indices obtained on the same fibres before treatment. The ordinate shows the pH of the exposure.)

The results show that exposure to low pH values (pH < 2) causes permanent weakening of the fibres by up to 30% of their original strength.

Discussion

The results of this investigation indicate that exposure to low pH values induces some drastic structural changes in hair. The exact nature of these changes is not clear but it appears that it does not involve fission of the main polypeptide chains.

The time dependence of the acid uptake curve (i.e. long delay followed by a sudden change) suggests that the processes responsible for the observed phenomenon are of a cooperative nature. A possible explanation is that the prolonged exposure to acid induces the rupture of bonds, strategically situated in the keratin fibre, as a consequence of which a rapid opening up of regions, hitherto inaccessible to acid penetration, follows. When investigating the supercontraction of wool, induced by LiBr, Crewther (5) came to the conclusion that the second stage of the super-contraction can be induced by dissociating acid-labile groups which exist in virgin keratin fibres. He suggested that these groups are disulphide linkages, which are under stress in the native protein fibre, and consequently highly susceptible to chemical attack. Benesch and Benesch (6) showed that simple, low molecular weight disulphide compounds undergo dissociation in strong acids (6M HCl) according to the following reaction scheme:

$$\text{R-S-S-R} + \text{HCl} \rightarrow \left[\begin{array}{c} \text{H}^+ \\ | \\ \text{R-S-S-R} \\ \text{Cl}^- \end{array}\right] \rightarrow \text{RS}^+ + \underset{\text{Cl}^-}{} \text{HS-R} \quad \ldots (\text{I})$$

Furthermore, Crewther (5) also suggested that in the case of the stressed disulphide bonds of keratin fibres it is highly probable that the reaction even occurs at values around pH 1, thus accounting for acid lability of some disulphide bonds. Our results are in general agreement with this hypothesis and lend further support to it. The absence of the changes in acid-treated hair, such as are induced in virgin hair by exposure to acid, and the diminishing of the rate of disulphide reduction in acid treated hair (the lowering of the rate of disulphide reduction observed in acid treated hair suggests that the reactive disulphide bonds amount in virgin hair to about 6% of the total disulphide content), and the reduction in the value of I_{20}, all support the above model. The acid-labile disulphide bonds, once dissociated, will not recombine again, or at least not in the same way as they existed in the virgin fibre, especially if their configuration in the virgin fibres is not thermodynamically the most favoured one.

It is highly probable that during the growth of the fibre, internal

stresses are built in which are stabilised at the last stages of the biosynthesis of the hair fibre by formation of interpeptide chain disulphide cross links. A severance of these cross links by acid would give an opportunity to the polypeptide chains in the acid-treated hair to take up a thermodynamically more stable configuration resulting in a rearrangement of the S-S cross-link distribution. A process of this kind would result in changed mechanical properties, manifested by the work to stretch and hysteresis indices, and also in a disappearance of the disulphide bonds of higher than average reactivity. (It is unlikely that a reforming of the stressed, reactive disulphide bonds will occur under the conditions which will prevail in the fibre after the removal of acid; on the contrary, it is more probable that some of the dissociated half cystine groups will not reform to disulphide linkages)

The nature of the newly exposed acid binding groups constitutes a difficult problem, especially since at pH 1.2 all the conventional acidic groups in keratin, i.e. COOH are protonated. One possible explanation is that at these low pH values the hydrogen bonded peptide groups (such as exist in a α-helices), will interact with HCl. Evidence for this exists from the titration curve of nylon (7), where considerable acid uptake has been observed at low pH values. The acid uptake below pH 1 was attributed to interactions between the peptide groups and HCl, possibly involving a "quaternization" of the N atom.

(*Received: 7th June 1967.*)

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J. Soc. Cosmetic Chemists **18** 651-662 (1967)

The quantitative estimation of the detergency and allied properties of shampoos in practice

S. V. BRASCH and MISS J. A. AMOORE*

Presented at the Symposium on "Product Testing", organised by the Society of Cosmetic Chemists of Great Britain in Eastbourne, Sussex, on 15th November 1966.

Synopsis—A method is described whereby small bundles of standard wool yarn, spun in the grease, are tied to the underside of the phalanges of a hairdresser's fingers and the weight loss determined after the completion of a shampoo under specific conditions. Detergent retained by the wool under these conditions may also be estimated. The results indicate how this method might be used to study the mechanism of the shampoo operation and the variable effects it produces, even under controlled conditions. The use of this method is also suggested as an aid in the evaluation of specific products. Implications of the type of results obtained are briefly mentioned.

Introduction

Assessment of various properties of shampoos under practical conditions is generally made subjectively. Thus, where a hairdressing salon is available, the hairdresser is able to obtain an impression of the lather formed during washing, by feel, and may subsequently judge, by eye, such features as "fly away" and gloss, whilst combing the dry hair, and on the final coiffure. Various methods of scoring may be used to compare these properties from one product to another.

It is extremely difficult to obtain fully quantitative measurements of shampoo properties or associated parameters, under completely practical

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conditions. This is due to the complexity of the physico-chemical factors making up these properties and the apparatus needed to measure them.

A relatively simple technique giving some quantitative indication of the behaviour of a particular shampoo in practice is therefore desirable, even if the information obtained therefrom covers only a limited aspect of the total properties of a shampoo.

Direct detergency measurements on shampoos or their detergent bases under practical conditions may be used as indicators of some of the ways in which they behave. Such measurements have the additional advantage of being quite readily carried out and they may also be used to evaluate some of the controllable factors in shampooing.

Experimental

The method is based on the gravimetric estimation of removable soil from A.A.T.C.C. standard wool yarn, spun in the grease (1), obtainable from the Lowell Textile Institute, Lowell, Mass., U.S.A.

The total soil content of the yarn was found by taking samples (0.5g) at intervals throughout each of two skeins weighing 1 kg and extracting (4 hr) in turn with ether and alcohol, followed by repeated washing in distilled water at room temperature. The weights of the samples were determined before and after the treatment, after drying to constant weight in a vacuum oven at 65°C over phosphorus pentoxide. Drying to constant weight under these conditions generally took five hours. Weight loss was expressed as a percentage of the dry, soiled weight. The figures below show the results obtained on the actual material used, together with the number of samples taken. The Standard Deviation of the results is also given. The two skeins came from deliveries about three years apart so that the figures also show the uniformity of the material over a period of time.

Percent Removable Soil in A.A.T.C.C. Wool

Skein (1)	*Skein (2)*
10.00 (S.D. = 0.52)	9.66 (S.D. = 0.26)
(Mean of 11 results)	(Mean of 6 results)

Grand Average = 9.83 (S.D. = 0.41)

All detergency figures in the subsequent work were expressed as percentage weight loss of a particular sample, without further recourse to control determinations of total removable soil by extraction and washing. This appeared justifiable in view of the small spread of the above results for total removable material. Further justification for this step was afforded

by the results of preliminary experiments using controls, which showed no improvement of precision over those using no controls. The fact that certain major factors included in the experimental design (see below) were shown to be significant gave additional evidence that this procedure was sufficiently sensitive.

Lengths of yarn (25″ long, for convenience) in the form of bundles, were tied with string to the underside of the phalanges of the hairdresser's fingers, as close as possible to the finger tips. The hairdresser then carried out the appropriate shampoo on a subject's head, followed by rinsing. The yarn bundles were taken from the fingers and, after removal of extraneous strands of hair, were squeezed between tissues to remove most of the water. Finally, drying to constant weight was carried out, as described above. All weighings were done in small, well-stoppered bottles to prevent moisture uptake from the atmosphere.

Preliminary experiments assessed possible differences due to using either the right or the left hand for the shampooing and rinsing. Depending on the habit of the hairdresser, one or other hand will spend a longer time involved in the actual shampooing action, the other hand being used for some periods in turning taps and manipulating the rinsing hose, etc. No difference was found, however, between the use of the two hands. Nevertheless, the left hand was consistently used in subsequent experiments.

Certain other ancillary procedures needed standardisation to ensure minimum variability.

These included:—

(a) The concentration of shampoo solution on the head.
(b) The time of shampooing.
(c) The time of rinsing.
(d) The mechanical intensity with which the shampooing was carried out.

These factors were determined as follows:—

Concentration of shampoo solution

To find the concentration of shampoo solution one required to know the average amount of water retained by a head of hair immediately before the shampoo solution was applied. For normal salon tests, the quantity and concentration of a particular shampoo stock solution applied to a head is chosen arbitrarily. The amount of water retained by a head of hair was found by wetting the head with water from a 1000 ml cylinder, filled to the mark, and collecting the water in a bowl placed in the basin, under the

person's head. When the water had ceased to leave the head in a continuous stream and was limited to a relatively slow succession of drops the portion in the bowl was returned to the measuring cylinder and the volume noted. The difference between this and the initial 1000 ml was taken as the amount retained by the head of hair. Where 1000 ml was insufficient to wet the hair satisfactorily the operation was repeated with the same portion of water. An appropriate volume of shampoo stock solution was then added to give the final required concentration of shampoo on the head.

The average quantity of water retained by the hair of eighteen women, chosen at random was:

93 ml (S.D. = 38 ml).

The Standard Deviation is given in brackets.

Time of shampooing

The time of shampooing was noted from ten observations (using a stop watch) on each of two hairdressers during the course of their normal work. The minimum and maximum times used (for any single application) by either of them, were 1 min and 2 min. The time was measured from the instant the shampoo solution was put on the head.

Time of rinsing

The times of rinsing were determined similarly to the shampoo times, the extremes being 1 min and 2 min 15 sec.

Mechanical intensity of shampooing

The mechanical intensity of shampooing was found to have no effect on detergency. This was established by the subsequent factorial experiments in which extreme conditions of agitation with the hands were used. These conditions were, on the one hand, the minimum movement of the hairdresser's hand compatible with some agitation and on the other hand, the maximum speed and pressure compatible with the subject's comfort. No attempt was made to control the temperature, other than ensuring that the water coming from the hand hose was at 40°C ± 1°C.

The most suitable replication for each experiment was found to be the use of three models per condition of treatment and three samples of wool per model. Greater replication, either of subjects or samples, did not sufficiently improve the precision of results to compensate for the additional

inconvenience and time involved. In a number of experiments, where gross effects were expected or were the only ones of interest, initial replication was restricted to two subjects with two samples per subject. Where the results thus obtained showed only limited statistical significance (say, at the 95% level) the number of experiments could be readily increased until the required replication was attained to establish the significance of any particular conclusion.

All experiments were conducted on the basis of a factorial design since it was hoped to learn whether, and to what extent, shampoo time, rinse time, agitation, affected the detergency of a particular shampoo. For any one shampoo, determinations were thus carried out at the two extreme shampoo and rinse times as well as at the two extreme conditions of mechanical agitation.

All the products used were proprietary shampoos based on lauryl sulphate.

Results

Table I shows the results obtained for a series of experiments involving five different products, some used on a dirty head of hair and some used in a second application on a head of hair washed immediately before. Two columns for tolerance limits and replication are given, to indicate the extent to which the tolerance limits depended on the replication. The column "Whether between-subject variance" has been included to show that only in a small number of cases can the true experimental error (residual variance) be attributed to the use of different subjects. In most cases it arises between the finger/wool bundle combinations on the hand during any one shampoo.

The results from each experiment were subjected to an analysis of variance to determine the significance or otherwise of the various factors included in the experimental design, and the tolerance limits of the average values obtained. Both the significance of major factors and the tolerances were calculated with due regard to the true experimental error, i.e. whether it arose from subject to subject variance or sample-to-sample (within subject) variance.

Discussion

In the three cases 1, 2, 10, it can be seen that the results obtained were time-dependent. The first two of these, which were repeats of the same experiment carried out at an interval of three months, indicated that

Table I

Product	Experiment and condition of subject's hair	*Mean detergency (% weight loss of sample) at treatment time (shampooing) shown	Replication and tolerance limits (1)	Replication and tolerance limits (2)	Significance level of tolerance limits	Whether between subject variance
(a)	(1) Dirty hair	*1 min* 10.9 *2 min* 8.1	3 subjects; 1 sample/subject ±1.7%	3 subjects; 3 samples/subject ±1.3%	99%	Yes
(a)	(2) Repeat of (1) after 3 mths.	*1 min* 9.5 *2 min* 7.9	2 subjects; 2 samples/subject ±1.1%	3 subjects; 3 samples/subject ±0.7%	99%	No
(a)	(3) Repeat of (1) after 6 mths.	7.7	2 subjects; 2 samples/subject ±0.5%	3 subjects; 3 samples/subject ±0.3%	99%	No
(a)	(4) Repeat of (1) on clean hair	8.7	3 subjects; 1 sample/subject ±0.6%	3 subjects; 3 samples/subject ±0.35%	99%	No
(a)	(5) Repeat of (4)	8.3	2 subjects; 2 samples/subject ±1.8%	3 subjects; 3 samples/subject ±1.2%	95%	No
(b)	(6) Dirty hair	8.2	2 subjects; 2 samples/subject ±2.2%	3 subjects; 3 samples/subject ±1.8%	95%	Yes
(c)	(7) Dirty hair	8.3	3 subjects; 1 sample/subject ±0.4%	3 subjects; 3 samples/subject ±0.2%	99%	No
(d)	(8) Clean hair	8.2	3 subjects; 1 sample/subject ±0.9%	3 subjects; 3 samples/subject ±0.5%	99%	No
(d)	(9) Dirty hair	7.2	4 subjects; 1 sample/subject ±0.7%	3 subjects; 3 samples/subject ±0.57%	99%	No
(d)	(10) Repeat of (9)	*1 min* 7.8 *2 min* 8.5	2 subjects; 2 samples/subject ±0.8%	3 subjects; 3 samples/subject ±0.65%	99%	No
(e)	(11) Dirty hair	6.7	3 subjects; 1 sample/subject ±0.7%	3 subjects; 3 samples/subject ±0.4%	99%	No
(e)	(12) Repeat of (11)	7.8	2 subjects; 2 samples/subject ±0.6%	3 subjects; 3 samples/subject ±0.4%	99%	No

*where no specific time is given the single figure shown indicates that the detergency was not time-dependent within the range studied

some soil redeposition took place during the course of the second minute of shampooing. A further repeat of the same experiment, carried out after another three months, no longer showed this effect. There may be many reasons why soil redeposition should take place on some occasions and not on others, but this is not relevant to the present subject matter. However, it is important that such effects are directly measurable and that they are shown not to happen consistently even with the one product. This is clearly an important consideration in such matters as hair conditioning studies where many effects may depend on the amount of soil remaining on the hair. To some extent these figures show why any long-term assessment of hair conditioning effects in practice is so difficult since, apart from the enormous random variation of hair from one person to another, the behaviour of the whole shampoo and allied system itself is so irregular, under the same nominal conditions. In experiment 10 greater cleansing occurred at the higher shampoo time, the effect showing significance at the 99% level, with sufficient replication. Again, at the 99% level, these results differ significantly from those of the same experiment done earlier. A similar effect is shown by experiments 11 and 12.

Extension of technique to measurement of other properties

The technique has also been used to assess the amount of detergent irreversibly retained by hair as a result of shampooing. Thus, after the gravimetric assessment of soil loss, an appropriate weight of the wool sample (about 0.015g) was subjected to a suitable procedure for the extraction and estimation of micro quantities of anionic detergent from protein (2). Percent detergent retained was expressed on the basis of dry, clean wool.

Results

These are shown in *Table II*.
Product (f) was *Sipon WD* (sodium lauryl sulphate found better than 99.9% pure).

Discussion

In the case of product (f), used on greasy wool, only the time of shampooing played any significant part in determining the amount of detergent retained. Where the experiment was repeated with wool which had previously been solvent extracted the rinsing time also governed the

Table II

Product	Conditions of treatment		Condition of wool	Detergent retention (wt.% on clean, dry wool)	Replication and tolerance limits	Significance level of tolerance limits
(f)	*Shampoo time* 1 min 2 min	*Rinse time* 1 min and 2 min 1 min and 2 min	Greasy Greasy	0.26% 0.31%	3 subjects; 3 samples/subject ±0.04%	99%
(f)	1 min 1 min 2 min 2 min	1 min 2 min, 15 sec 1 min 2 min, 15 sec	Clean Clean Clean Clean	0.39% 0.36% 0.50% 0.38%	3 subjects; 3 samples/subject ±0.10%	99%
(b)	1 min and 2 min	1 min and 2 min, 15 sec	Greasy	0.15%	3 subjects; 3 samples/subject ±0.1%	95%

amount of detergent left. However, three of the four combinations of conditions gave effectively the same result and only when a long shampoo time was followed by a short rinse time was there a significant increase in the detergent remaining on the wool.

With product (b) no effect of shampoo time or rinse time was discernible at the replication used. However, one can see that, at least in some cases, net detergent retention may be strongly influenced by the presence or absence of soil on the hair and that the extent of this retention may be governed by the conditions of shampooing and rinsing.

Conclusion

Quantitative assessment of shampoo properties and behaviour under completely realistic conditions are extremely difficult. Under such conditions soiled hair itself would have to be used and, ultimately, hair clippings straight from the head. This clearly introduces problems of the uniformity of the material studied (namely, the hair) as well as in the development of techniques suitably refined to measure any changes in the hair which could be interpreted in a meaningful way. The approach described in this paper, although not completely realistic (in that wool is used on the hands, rather than hair on the head), is believed to be a reasonable initial compromise between manageable technique and the use of actual conditions.

Notwithstanding the difficulties involved in using soiled hair clippings, or taking samples from a head during the course of a shampoo, an attempt to adapt the method to the use of hair itself might prove worthwhile.

Acknowledgement

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Introduction by Mr. Brasch

The work reported here arose out of various attempts to study some of the fundamental aspects of hair conditioning and the mechanisms involved, with due regard to the practical conditions under which shampoos are used. There is quite a deal of published work on laboratory results concerning the physico-chemical behaviour of a whole range of compounds in relation to hair, as well as a whole legion of results of similar type of work done on wool. Such results on wool are often used as the basis of discussions about the actions of shampoos, whether conditioning or otherwise.

It seemed to us that one useful first approach would be to choose some simple variables which are easily estimated and to use these to test whether some of the factors which one would expect to operate during shampooing do in fact do so to any significant extent. After all, one would expect the intensity of shampooing, that is to say the degree to which you rub the head, to bear some relation to the amount of soil removed from the hair and again it would seem obvious to suspect that time of shampooing and time of rinsing play some important part.

At the outset we wanted to obtain some measure of the effect of these factors. There are quite a number of variables which could be measured, some of which require fairly sophisticated techniques. We chose detergency and detergent retention but these are by no means the only variables which are measurable after shampooing nor indeed are they the only relevant ones for an understanding of conditioning effects. Surface characteristics of hair, rigidity-modulus and various other things obviously also play a very important part. In a system as complex as that existing on the head during the course of a shampoo one can reasonably accept the fact that there is bound to be a gap, as it were, between an actual situation on the head and the way it is assessed by the particular technique. This gap is bound to exist no matter how sophisticated the technique used to study these effects and how many factors are thought to have been taken into consideration in devising the technique.

We suspected that in a study such as this the main causes of variation would lie in the system itself and that such a variation would not justify the use of techniques designed to measure very sensitive changes in behaviour. In choosing a quantitative assessment it seemed better, at least to start with, to err on the side of simplicity. In the conclusion of the paper we suggest the extension of this technique and the whole approach to the use of hair itself. We have followed this up to some extent, although unfortunately circumstances did not allow us to continue to study it as fully as we would have wished. Nevertheless, the results we did obtain on hair are to be published (3). An interesting feature which arises out of the further work and in line with some results obtained by Ester and Longfellow (4) is the relatively small amount of fatty matter removed from hair during shampooing, something like 40% of the original amount present on the hair. This obviously points to the need for care in interpreting the sort of results we obtained using wool bundles because our wool bundle technique did, in fact, give us very much higher figures for the removal of fatty matter by shampooing.

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DISCUSSION

MR. K. V. CURRY: 1. What is "wool spun in the grease"? 2. Is the grease a mineral oil?

MR. BRASCH: 1. It is the same wool which Barnett and Powers used in their original laboratory work. 2. Just natural wool fat. It is easily recognisable from the smell of the yarn.

MR. K. V. CURRY: Have you studied your wool fats before and after the shampooing process to see whether there is any build-up of specific components in the residue as opposed to the original?

MR. BRASCH: No, but in the subsequent work (3) we cut a bit of hair off a person's head, did some tlc runs on the ether and alcohol extracts therefrom, and after the shampoo did the same thing with a batch of hair next to this. From a qualitative point of view, we found only relatively few components removed, although there was some quantitative removal of each component.

MR. K. V. CURRY: I think most of this work describes single applications. Do you get any more off with successive treatments?

MR. BRASCH: We have never tried a double application. Although the figures quoted here are absolute percentages of fat removed, they represent something like a 98.5% loss of fatty matter as a result of one shampoo.

MR. K. V. CURRY: Could this technique be applied using the familiar half-head technique where you have, say, skeins of wool washed with one product, and skeins washed in the other?

MR. BRASCH: I would say yes.

MR. E. W. CLARK: I wish to mention a point of interest concerning the use of raw wool for assessing the detergency. If it is truly all wool with a natural grease on it, it will also have other organic secretions, i.e. the dried sweat which is highly surface active and is capable of degreasing the wool almost entirely on its own even by soaking in hot water. Could this not lead to false interpretations of results?

MR. BRASCH: In a sense, you are right. If there is any value in this method it lies in using it as a comparative method. For instance, if one wants to compare two detergents which are suspected of giving widely different effects. One would get a comparison and it does not seem to me to matter greatly whether the absolute figures are inflated by virtue of the effects you mentioned provided, of course, one bears your criticism in mind.

MR. E. W. CLARK: Is the wool of a standard quality? Different qualities of wool can vary temendously in the ratio of grease to other matter.

MR. BRASCH: It is of a standard quality in the sense that it is supplied as a standard product for testing purposes by the Lowell Textile people in America, and I have given figures for the grease removal as a result of extraction from two different skeins. I believe the delivery of the skeins in our case was something like three to five years apart. We had a large stock in the laboratory from some previous work and then again, more recently, brought in some more. In the case of the early skein, for instance, we found 10% by weight of removable fatty matter whilst the skein

received five years later contained 9.66%. It seems to me that this small difference is indicative that it is a fairly standard product over many years.

MR. E. W. CLARK: Yes, unless you have compensating errors of some kind, because the degree of autoxidation of wool fat can have quite a large effect upon its ease of removal. In the finely divided form on the wool fibres autoxidation is quite rapid. In five years there would be a high degree of autoxidation.

MR. BRASCH: I appreciate that. This does not seem to have had any drastic effect on the ease of quantitative removal of the fat from the wool. I cannot vouch for the fact that there may not have been some oxidation inhibitor of some sort included during the preparation of the yarn.

MR. E. W. CLARK: In the test it might pay to have a standard shampoo formulation to assess the wool sample itself.

MR. BRASCH: Yes, indeed. Our standard baseline was merely the solvent extractability, but I agree that a standard shampoo in addition may be very valuable.

MR. K. V. CURRY: Have you repeated any of this work using hair? Do you get the same high detergency with hair as you do with wool?

MR. BRASCH: We have not repeated this on hair in quite the same way because it is very difficult to get a large quantity of hair to use over a long period of study which is as uniform as standard prepared wool, for example. Quite apart from this, to tie or devise some means of holding hair in a bundle of one form or another on the fingers is very difficult indeed. We did try wrapping hair up in cushions made from gauze, but this seemed to be getting a little remote from practice. We therefore did not pursue this. As I mentioned above, we used a similar approach if not an identical technique. We took various female models and selected parts of the hair near their necks so when we cut off approx. 0.5g it would not show. This was done both immediately before and after shampooing, the samples of hair being next to each other. The residual amount of fatty matter was quantitatively estimated by solvent extraction. We only achieved a removal of something like 40% of the fat from the hair as opposed to something like 98% when we used wool.

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The potential irritancy to the rabbit eye mucosa of commercially available cream shampoos

R. E. DAVIES and K. H. HARPER*

Presented at the Symposium on "Product Testing", organised by the Society of Cosmetic Chemists of Great Britain in Eastbourne, Sussex, on 15th November 1966.

Synopsis—A study has been made of the irritancy to the rabbit eye mucosa of five commercially available cream shampoos, employing four different screening procedures. It is concluded that all five shampoos are "irritants" to the rabbit eye mucosa. Three show severely irritant properties and one other clearly falls under suspicion in this respect. Results obtained by the different methods are discussed.

Introduction

In 1963 two of us from this laboratory were privileged to address this Society on the question of the reactions elicited in the rabbit eye on application to the cornea and conjunctivae of a selection of commercially available shampoos (1). Although the primary purpose of that talk was to present comparative data produced by several methods of assessment, we also drew attention to the fact that the two cream shampoos tested were considerably more irritant than any of the liquid formulations. We observed, however, that prior dilution of the cream shampoos with water – to a concentration of 10% – minimised the irritancy in one instance, and exaggerated it in the other. As a general rule, other tests with cream formulations (not reported at that particular meeting) confirmed that a diluted form of the cream shampoo exhibited greatly reduced irritancy under the conditions of the test, and the question of whether or not prior

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dilution of the shampoo might provide a more practical assessment of the user hazard came up for discussion in the Toxicology Subcommittee of this Society. However, at that time it was acknowledged that the paucity of the data on experimental animals precluded the drawing of any real conclusion and the question was left in abeyance until such information should be made available.

The purpose of this communication is therefore twofold. In the first instance we wish to report on the reaction of the rabbit eye mucosa to a selection of cream shampoos currently available in this country. In the second, we wish to continue our comparison of the different test methods for appraising irritancy.

Experimental details

Five cream shampoos were purchased from shops in Huntingdon, coded as shampoos A to E and all identifying marks removed. The code was not broken until completion of the investigation.

A total of 18 rabbits of a New Zealand White strain was used to test each sample. The procedure followed was identical with that used in the earlier studies (1).

Rabbits 1- 6: Sample instilled, no further treatment.
Rabbits 7-12: 10% dilution of sample instilled, no further treatment.
Rabbits 3-15: Sample instilled, eye irrigated with 20ml water at 2 sec.
Rabbits 16-18: Sample instilled, eye irrigated with 20ml water at 4 sec.

(a) Rabbits 1 - 6 provided the design for the "FDA test".
(b) Rabbits 1, 2 and 4, plus rabbits 13-15 and rabbits 16-18, provided the design of the "Draize test".
(c) Rabbits 7-12 provided an assessment of the effect of dilution of the sample (dilution test).
(d) Rabbits 3 and 5, together with rabbits 16 and 18 represented the abbreviated Draize test used on occasions by us as a preliminary screen (HRC screen).

In all cases the eyes were scored by the system devised by Draize (2). In interpreting the results obtained we used the following arbitrary classification in addition to the irritancy definitions given by the official test procedures.

1. Non-irritant – no reaction at any time.
2. Slightly irritant – reaction confined to the conjunctivae and persisting for up to 5 days only.

3. Mildly irritant – conjunctival reaction, accompanied by slight corneal and/or iridial reaction (maximum score of 5), the latter persisting for up to 5 days.
4. Moderately irritant – conjunctival reaction accompanied by moderate corneal and/or iridial reaction (maximum score of 10), the latter persisting for up to 5 days.
5. Severely irritant – conjunctival reaction accompanied by more persistent and severe injury to the cornea and/or iris (score above 10), effects persisting for more than five days.

Results

To facilitate comparison between results obtained by the different test procedures, the data have been expressed as mean values per rabbit and are listed for each shampoo in *Tables I–V*. Significant deviations from the mean value in the case of individual animals are referred to in the text that follows.

Table I
Mean scores/rabbit of reactions elicited by shampoo A

Test	No. of rabbits	Days after treatment					Days of maximum persistence
		1	2	3	4	7	
(a) FDA	6	11	13	13	13	8	134+
(b) Draize							
Unwashed	3	11	15	17	15	7	15
Washed at 2 sec	3	8	5	3	3	0	4
Washed at 4 sec	3	9	5	4	3	0	4
(c) Dilution	6	9	6	4	2	<1	7
(d) HRC screen							
Unwashed	2	11	11	11	13	14	134+
Washed at 4 sec	2	9	6	4	3	0	4

Table II
Mean scores/rabbit of reactions elicited by shampoo B

Test	No. of rabbits	Days after treatment					Days of maximum persistence
		1	2	3	4	7	
(a) FDA	6	16	10	8	4	1	7
(b) Draize							
Unwashed	3	15	10	7	4	1	7
Washed at 2 sec	3	7	5	2	2	<1	7
Washed at 4 sec	3	6	3	1	0	0	3
(c) Dilution	6	9	5	3	2	<1	7
(d) HRC screen							
Unwashed	2	11	11	9	4	3	7
Washed at 4 sec	2	6	3	2	0	0	3

Table III

Mean scores/rabbit of reactions elicited by shampoo C

Test	No. of rabbits	Days after treatment					Days of maximum persistence
		1	2	3	4	7	
(a) FDA	6	12	10	8	7	7	40
(b) Draize							
Unwashed	3	13	9	6	7	9	40
Washed at 2 sec	3	9	4	3	2	0	4
Washed at 4 sec	3	6	4	3	1	0	4
(c) Dilution	6	8	4	2	1	< 1	7
(d) HRC screen							
Unwashed	2	13	12	8	8	7	40
Washed at 4 sec	2	6	4	4	2	0	4

Table IV

Mean scores/rabbit of reactions elicited by shampoo D

Test	No. of rabbits	Days after treatment					Days of maximum persistence
		1	2	3	4	7	
(a) FDA	6	11	9	12	7	6	70
(b) Draize							
Unwashed	3	11	7	11	5	3	17
Washed at 2 sec	3	4	< 1	0	0	0	2
Washed at 4 sec	3	6	2	0	0	0	2
(c) Dilution	6	5	2	1	0	0	3
(d) HRC screen							
Unwashed	2	11	13	14	11	11	70
Washed at 4 sec	2	5	1	0	0	0	2

Table V

Mean scores/rabbit of reactions elicited by shampoo E

Test	No. of rabbits	Days after treatment					Days of maximum persistence
		1	2	3	4	7	
(a) FDA	6	12	10	8	6	6	45
(b) Draize							
Unwashed	3	11	9	7	4	3	9
Washed at 2 sec	3	2	2	1	0	0	3
Washed at 4 sec	3	3	2	< 1	0	0	3
(c) Dilution	6	8	8	4	3	1	7
(d) HRC screen							
Unwashed	2	12	11	9	8	11	45
Washed at 4 sec	2	4	3	1	0	0	3

Shampoo A

FDA test: Four rabbits gave a positive reaction. Each animal showed temporary iritis and partial eversion of the eyelids and in two rabbits there were corneal opacities, one of which was still present 134 days after application of the shampoo.

Draize test: In the three eyes that remained unwashed after treatment, one developed a temporary corneal opacity and all three showed iritis and partial eversion of the lids. Irrigation with water alleviated the severity of the response which was confined to the conjunctivae.

Dilution test: One rabbit showed a positive reaction with partial eversion of the eyelids. In the remaining animals, mild conjunctival reaction only was observed.

HRC screen: Corneal opacity, which was still present on day 134, temporary iritis and considerable conjunctival reaction with partial closure of the eyelids was observed in one of the eyes that remained unwashed after treatment. In the second unwashed eye, mild conjunctival reaction only was observed. In the washed eyes, reaction was confined to the conjunctivae.

Interpretation:

Shampoo A is defined by the FDA test as an "eye irritant" and by the Draize test and HRC screen as a severe eye irritant. Dilution to 10% and irrigation with water clearly reduce the irritation response.

There was, therefore, good agreement between the different test procedures with this shampoo, except that the dilution test obviously did not reveal the full potential irritancy of the shampoo.

Shampoo B

FDA test: Five rabbits gave a positive reaction. Each animal showed partial eversion of the eyelids and in three there was temporary iritis. In the remaining rabbit, reaction was mild and confined to the conjunctivae.

Draize test: In the three eyes that remained unwashed after treatment, two showed temporary iritis and all three showed partial eversion of the eyelids. In the eyes irrigated with water, mild conjunctival reaction only was observed.

Dilution test: None of the rabbits gave a positive reaction. Reaction was mild and confined to the conjunctivae.

HRC screen: Partial eversion of the eyelids was observed in one of the eyes that remained unwashed after treatment. In the second unwashed eye

and both washed eyes mild conjunctival reaction only was observed.

Interpretation:

Shampoo B is defined by the FDA test as an "eye irritant", but is not considered to be a severe irritant in the Draize test. By our own arbitrary classification, it is categorised as mildly irritant.

Again, as with Shampoo A, there was good agreement between the different test procedures, and the dilution test did not reveal the full potential irritancy of the shampoo.

Shampoo C

FDA test: Five rabbits gave a positive reaction. Corneal opacities, both of which persisted until day 40, were observed in two rabbits, and all five animals showed temporary iritis. In two rabbits there was partial eversion of the eyelids.

Draize test: Corneal opacity was observed in one of the eyes that remained unwashed after treatment and all three unwashed eyes showed temporary iritis and mild conjunctival reaction.

In the washed eyes irrigation with water clearly reduced the irritancy response and mild conjunctival reaction only was observed.

Dilution test: One rabbit showed a positive reaction with partial eversion of the eyelids. In the remaining animals mild conjunctival reaction only was observed.

HRC screen: Corneal opacity, temporary iritis and partial eversion of the eyelids were observed in one of the eyes that remained unwashed after treatment. In the remaining unwashed eye and those irrigated with water mild conjunctival reaction only was observed.

Interpretation:

Shampoo C is defined by the FDA test as an "eye irritant" and by the Draize test as a severe irritant. By our own arbitrary classification system the shampoo is categorised as moderately to severely irritant. The irritation was reduced in those eyes irrigated with water, and in those treated with the 10% dilution.

Once again there was good agreement between the different test procedures, with the dilution test again failing to demonstrate the potential irritancy of this shampoo.

Shampoo D

FDA test: Five rabbits gave a positive reaction. Corneal opacity devel-

oped in two eyes and persisted in one for 70 days. Four rabbits showed temporary iritis and in two there was partial eversion of the eyelids.

Draize test: In the eyes that remained unwashed after treatment, one developed temporary corneal opacity and iritis, a second showed temporary iritis, and in the third there was partial eversion of the eyelids. In the washed eyes, irrigation with water clearly reduced the irritancy response and slight conjunctival reaction only was observed.

Dilution test: Slight conjunctival reaction only was seen.

HRC screen: Corneal opacity, temporary iritis and partial eversion of eyelids were observed in one of the eyes that remained unwashed after treatment but in the second eye reaction was mild and confined to the conjunctivae. In the washed eyes slight conjunctival reaction only was observed.

Interpretation:

Shampoo D is defined by the FDA test as an "eye irritant" and by the Draize test as a severe eye irritant. In our own classification system the shampoo would be categorised as moderately to severely irritant.

Once again there was good agreement between the different test procedures, with comment regarding the dilution test as for the preceding samples.

Shampoo E

FDA test: Four rabbits gave a positive reaction. In one there was opacity of the cornea which persisted until day 45. In this animal, and in one other, there was temporary iritis. Three rabbits showed partial eversion of the eyelids.

Draize test: Two of the eyes that remained unwashed after treatment showed partial eversion of the eyelids, but in the third there was only mild conjunctival reaction. Irrigation with water clearly reduced the irritancy response and slight conjunctival reaction only was observed.

Dilution test: Mild conjunctival reaction only was seen.

HRC screen: Corneal opacity, temporary iritis and partial eversion of the eyelids was observed in one of the unwashed eyes, but in the second the reaction was mild and confined to the conjunctivae. In the washed eyes slight conjunctival reaction only was observed.

Interpretation:

Shampoo E is defined by the FDA test as an "eye irritant" but it is not considered by the Draize test to be a severe irritant. According to our

classification system, this shampoo is categorised as moderately to severely irritant.

It can be seen that the Draize test and the dilution test failed to show the iridial damage that was revealed by the FDA test and, fortuitously, by the HRC screen. Corneal damage was an atypical reaction, and was observed in only one rabbit.

Discussion and conclusions

These studies confirm earlier observations from this laboratory that cream shampoo formulations are to be regarded as eye irritants when tested according to accepted procedures. The degree of irritancy produced, however, varies appreciably ranging from the severe responses elicited by A, C and D, to the relatively mild reaction produced by shampoo B. In general, the results obtained confirm our earlier observations (1) that cream shampoos are more irritant than are the liquid varieties.*

The study also provides clear evidence that a 10% concentration of the cream is much less irritant than is the cream itself, and of course we believe that this fact will be duly noted by those proponents who consider that prior dilution of the shampoo provides a more practical assessment of user hazard. According to one participant at the 1963 Symposium, a cream shampoo marketed by his company elicited no complaints in two years during the marketing of approximately 35 million doses. We must assume that "complaint" in this particular instance would apply to relatively severe reaction, perhaps necessitating medical treatment, and it is probable that minor degrees of scalp irritation would remain unreported.

We also believe that the stinging sensation and possible conjunctivitis caused by accidental contact of the eye with the cream or suds would be regarded as "normal" by the average user, and again there would probably be no formal complaint to the manufacturer unless vision was temporarily or permanently affected. How many of us, for example, report to a soap manufacturer the very painful reaction when we "accidentally" get soap in our eyes.

We believe, therefore, that undue significance should not be attached to the absence or low incidence of user complaints, although this fact must of course be reassuring in so far as it probably indicates freedom from seriously adverse properties.

The same opinion regarding the value of user complaints has been

* It is hoped that additional data to support this will be available in time for the meeting.

advanced somewhat more forcefully by Maibach and Epstein (3) who aver that "just as most of the volume of an iceberg hides beneath the surface, complaint letters indicate but a minute fraction of the total problem".

If this view is correct, then in the interest of public safety we must be guided, to a great extent, by the outcome of our experimental tests – why else do them? – and in this instance they tell us that all of the creams tested are potentially irritant to the eye mucosa, some dangerously so; it follows, therefore, that unless appropriate remedial steps are taken to remove any neat shampoo that is accidentally instilled into the eye, there is a theoretical danger of ocular damage associated with use of these formulations.

The animal tests then expose the potential risk to the user. The manufacturer must weigh this theoretical risk against his assessment of the danger in practice and decide whether or not a user hazard is indicated. Since all of the five products tested in the present study presumably enjoy a successful commercial life, it must be assumed that the manufacturers have decided correctly.

Comparison of the results obtained with the various test procedures again indicates that the best cover is provided by the 6 rabbit FDA Test. We still maintain, however, that inclusion of an additional group of, say, three rabbits, in which the eye is irrigated with water, is necessary to safeguard against the rare occurrence of increased irritancy resulting from the procedure. We ourselves have experience of one such product (1) and Levenstein (4) has drawn attention to the fact that with 0.1% sodium lauryl sulphate "you have the lowest activity, the greatest reaction, and most trouble". In all cases that we have studied, prior dilution of the cream shampoo has clearly failed to allow the full irritancy potential of the cream to be realised. In this respect, therefore, it may be considered to provide a relatively insensitive test procedure. It does not follow, however, that it is of no value as a predictive test and it is arguable that it does in fact provide the more practical assessment of hazard under normal user conditions.

At this point the dilemma is all too obvious. Do we follow the normal pattern of classical toxicology and select the test that provides the most stringent conditions and allows the full toxicity of the product to be made apparent, or do we merely seek an animal model that attempts to simulate as closely as possible the conditions of practical usage. Fortunately, it is not the purpose of our communication to debate this problem since in our title we have been most careful to refer to "potential irritancy".

However, we cannot ignore the question completely and would like to take this opportunity to express our belief that assessment of risk can only

come from a full understanding of the intrinsic toxicity of a material. Further tests may then be required to assess safety-in-use under specified conditions, but at least we should be fully aware of any damage the compound is capable of causing.

According to Calnan (5) "every manufacturer of a therapeutic or cosmetic product takes a calculated risk (though he may not always be conscious of it) when he puts his product on the market". Our tests clearly place cream shampoos within the same category.

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DISCUSSION

MR. C. PUGH: I think it is important to take into account the physical characteristics in assessing the relation between rabbit tests and human experience. In the last eight years I have seen three letters from people who have accidentally splashed liquid shampoos into their eyes. Each of them has described their reactions rather like a mild irritation in the Draize test, but they all cleared up within three or four days. Although sales of thick cream shampoos are high enough to produce this sort of result, I have not yet seen any letter from a user of a cream shampoo complaining of getting it in their eyes. I am sure this is because it is much more difficult. It is fair to say that shampoo users in general either dilute their shampoos, or dunk their hair in water and then apply the neat shampoo. In these conditions it is much more difficult to get a cream shampoo into the eye than a liquid one. Cream shampoos may be more irritant in the Draize test, but in use they are probably less of a hazard than liquid shampoos.

MR. R. E. DAVIES: We can but agree with you. Our preliminary studies indicate that the physical nature of a shampoo is an important contribution to its safety-in-use. It is certainly reassuring to hear that cream shampoos in general use do not present a hazard. I would stress, however, that as toxicologists we are also interested in the potential irritancy of a shampoo. We have to bear in mind that people are using these shampoos possibly directly from the bottle, and there is the chance that some may accidentally enter the eye in an undiluted form. A function of the rabbit test is to indicate the type of reaction that can be produced by a shampoo entering into the eye.

We always regard your comments about consumer complaints with some interest, although unfortunately these data are not generally made available to us, and therefore we are not in a position to comment further on your findings. Nevertheless, it is

comforting to realise that man finds the shampoos much safer than the rabbit finds them.

MR. N. J. VAN ABBÉ: It is extremely valuable to have this comparison of commercial products, but I do feel that it is quite possible to draw the wrong conclusions from it, and I would suggest that rather different conclusions can be drawn than are drawn in the paper. The fact that no complaints have been received by us on cream shampoos in the eye cannot be taken to mean that neat shampoo never gets in the eye. For instance, I feel that with the use of plastic tubes which occasionally splatter, some sufferers of neat shampoo in the eye must have appeared in the course of the years. If the reactions that they have suffered bore any resemblance whatever to the reactions in the rabbit, I feel quite certain that we would have known about it because we do know of things much less severe. Maybe the actual numbers of complaints do not represent the true figure in the whole population, but I cannot believe that anything resembling the severity produced in the rabbit occurring in a human would go unreported to the manufacturer. No such reports have appeared, and to my mind this means that the results obtained in the eye test are in some measure purely specific to the rabbit. I think that this is not unreasonable because I believe I am right in saying that lacrimation in the rabbit does not resemble lacrimation in the human eye. What I would be inclined to say is that the 10% test in the eye is a reasonable approximation to safety-in-use. This is the most likely occurrence during normal usage of a shampoo, whether cream or liquid. The neat applied test followed by washing, as in the original Draize procedure, seems to me to represent what happens when a human subject accidentally gets neat cream shampoo in the eye – either it is washed out by tear secretion or by tap water within seconds. The response is essentially what you have reported in the Draize test with washing, which in fact is as mild, if not milder, than the effect from the 10% dilutions. I cannot help feeling that we are going beyond the bounds of reason if we regard the neat, unwashed application as being the ultimate toxicity. It would be if we were selling shampoos to rabbits, but I do not think it is so in selling them to humans.

MR. F. RIDGWAY: I cannot agree with Mr. Van Abbé that this test should be carried out only on the diluted shampoo. If you consider the case of a child who might accidentally receive the concentrated shampoo or cream in its eye and develop an intense reaction, the eyes may be closed, the reaction may not become apparent, and the eyes would not be washed. Again, a perhaps not very intelligent mother, might neglect to wash the child's eye, and it could be some time before hospital treatment was given. I therefore think that the test should be carried out with a concentrated shampoo because there are conceivably conditions in use where washing may not be carried out within a short time of its getting into the eye.

MR. R. E. DAVIES: There seems to be little doubt that consumer complaints do not indicate a hazard-in-use with cream shampoos. There have been two statements from the floor to support this. We would also agree that the rabbit eye test using undiluted shampoo does appear to indicate greater irritation than is seen in man. The dilution test may well be a more realistic assessment of safety-in-use, but my own feeling is that at the present time there is little scientific data either to confirm this or to indicate the correct dilution for any given class of products, such as the arbitrarily chosen 10% dilution for shampoos. I think it is unnecessary for me to stress the implications of "false negative" test results.

We should not overlook the fact that certain shampoo formulations have caused trouble in the past, and in this context I am thinking of the quaternary ammonium shampoos that were the subject of the famous FDA seizure in 1938. We are also aware of at least one example quoted by Rieger and Battista (6) of a product used as a neutraliser that was found to be innoxious in the rabbit test using the undiluted product, but which eventually proved to be an irritant to man.

With regard to the predictive value of the results obtained with exaggerated exposures, we would emphasise that the effects recorded in our study resulted from the instillation of $^1/_{10}$ ml of the shampoos as sold. This can hardly be described as an unrealistic exposure. I do not think that as a general premise we would accept Mr. Van Abbé's comments, because as toxicologists it is almost axiomatic that we should establish what damage the material, at worst, is capable of causing. As far as human reaction is concerned, there are occasions when this procedure provides misleading information. A good example of this is probably provided by DMSO which, when given at high dosage to animals, causes characteristic changes in the lens of the eye and yet apparently has no effect upon the human eye, even when given for more prolonged periods of time.

However, I am sure we all agree that current test methods involving animals are useful in the assessment of the safety of topical agents, provided the data is placed in its correct perspective. I think that these tests can yield valuable information relating new substances to others for which the hazards have been defined by both time and experience. Their use for predicting human responses in an absolute sense is tenuous at this present time. Many of us must feel that there is the greatest need for fundamental understanding of the mechanisms of injury and its causative factors. We may then be in a position to design more definitive and rational test procedures which, in turn, may increase their predictive value.

MR. N. J. VAN ABBÉ: I would say that the reactions obtained in the rabbit eye with neat shampoo are not tenuous in relation to human experience but totally wrong, and that either we are using the wrong test animal or using it in the wrong way. I agree that the dose is not an unreasonable one and I would imagine that it must have happened that humans have received considerably larger doses in their eyes. I just do not think they react in the same way.

In reply to Mr. Ridgway, I would say that this is most likely due to the fact that the tear secretion dilutes out the shampoo rapidly so that the response is nothing like that which is seen in the rabbit. Consequently I am saying, not that you should not test on rabbits, but that you should adopt the Draize procedure rather than leaving the neat shampoo in the eye.

MR. R. E. DAVIES: We do, in fact, add some support to this, although I would still stress the point that part of the value of the rabbit test is to relate the reactions seen with our new product to those observed with old or well-established products. On a comparative basis, it does have some value.

The subject of species variation is a very thorny one in that we do not know enough about the basic morphology and physiology of different species of animals. We can compare different animal species and find staggeringly different results to standard test procedures. There have been a number of publications during the past few years

(6) Rieger, M. M. and Battista, G. W. *J. Soc. Cosmetic Chemists* **15** 161 (1964).

to support this. Beckley (7) compared the rabbit, dog and monkey; Buehler and Newmann (8) compared rabbit and monkey; and Roudabush and Terhaar (9) compared rabbit and guineapig.

However, it is still not possible to conclude that any one species is the animal of choice. It may well be that the rabbit, which is a convenient laboratory animal, is as useful a species as any other, provided the data obtained is interpreted on a comparative basis.

I agree that the standard tests could be modified, and indeed many suggestions have been published. We are in agreement with the inclusion of animals in which the eyes are washed shortly after instillation of the test material. This is of definite value. The rabbit eye does respond differently to the human eye as regards the nature of its secretions. In the human eye watery "tears" are produced, but in the rabbit eye the watery secretions seen during the first, say 20 hr, are superseded by a white, viscous secretion. I do not know the exact significance of this, and would be grateful if anybody knows of any relevant publications. Nevertheless, this is obviously a different response to the test material. It is possible that some preparations we put into the eye may become bound to those secretions and thereby increase the period of corneal exposure.

MR. F. D. GRAINGER: Was there any correlation between the degree of irritancy experienced and the viscosity of the shampoos and/or the miscibility of those shampoos with the tear secretion? In other words, is the degree of irritancy in some way proportional to the degree of eradication of the irritant from the eye and was this looked into?

MR. R. E. DAVIES: We have not studied this problem in detail, although I hope we will eventually discover the cause of the irritation to the rabbit eye. This was not the subject of our brief. We simply took the five cream shampoos that were considered to hold the "lion's share" of the market at that time, and assessed their irritancy according to standard test procedures. However, we are now most interested in trying to find a causative relationship between the biological effect and the composition of the shampoos. At this time our results are too provisional to be of any value. There is no obvious relationship with the chemical composition of the shampoos, and it may be that the physical factors are more important. The viscosity of the shampoo, as we have already heard from Mr. Pugh, may well be an important feature, possibly reducing the chance of accidental entry into the eye.

MR. D. BASS: The discussions and conclusions claim that cream shampoo formulations are to be regarded as eye irritants. This is not true of all cream shampoo formulations, as it is possible to produce a cream shampoo using an amphoteric detergent which does not irritate or even sting the eye. Furthermore, it would be possible to reduce the high irritation of shampoos that have been tested in this paper by replacing a proportion of the detergent with an amphoteric. The work described is interesting but of little value unless it is correlated with the detergent used.

MR. R. E. DAVIES: I believe I have answered a certain amount of your question already. The purpose of our brief was not to correlate biological activity with the

(7) Beckley, J. H. *Toxicol. Appl. Pharmacol.* **7** Suppl. 2. 93 (1965)
(8) Buehler, E. V. and Newman, E. V. *ibid* **6** 701 (1964)
(9) Roudabush, R. L. and Terhaar, *ibid* **7** 559 (1965)

composition of the shampoos. I would agree with you that our experience with amphoteric detergents does suggest that they are less irritant. I can add that none of the shampoos tested here contained amphoteric detergent.

MR. W. S. BEACH: I assume that the shampoos that have been tested are the usual standard anionic type of sulphurated alcohols?

MR. R. E. DAVIES: I think you could accept that. The five cream shampoos, as we stated in our paper, were purchased from a local chemist's chop. They were all standard shampoo formulations.

DR. K. H. HARPER: I cannot accept Mr. Van Abbé's arguments that because they receive no complaints that a shampoo has caused damage in the eye, this indicates that it is not irritant. He made the assertion that the shampoo must get into the eye, and that this must indicate freedom from irritancy. I hardly feel that one can adopt any code of practice with this as the basic premise. One has to have a little more information than mere conjecture of this nature.

I think there is a close analogy with the paper by Brasch and Amoore (10). They have developed a method for testing detergency and find with this test something like 90% removal of fat. They do not say that because a compound has this effect it has severely detergent properties and therefore is of no value in a shampoo. Instead, they attempt to correlate this result with human experience. In other words, they have a model that they can interpret and, I think, the same is true of the rabbit eye test. One assesses the most severe reaction that a compound is capable of producing, and then needs to interpret this in terms of the possible human response. I think the Procter & Gamble people reported that in their experience materials producing primary irritation indices of the order of more than 2.5 invariably led to an increase in the number of consumer complaints. To me this seems a realistic approach to the problem. You draw a comparison with materials that you know to be irritant in human practice and ones that are not, and there the rabbit eye and the rabbit skin tests can be of predictive value.

MR. N. J. VAN ABBÉ: I would not like to suggest that the rabbit test has no relevance. I was referring to the way in which it is used and the extent to which you can draw conclusions. It does not seem to me that there is any evidence to suggest that the responses of the rabbit eye to neat cream shampoo are likely to correlate in any way with human experience. I do not believe that cream shampoos are not irritants to the human eye because we have not received any complaints.What I believe is that the responses obtained by cream shampoos in the human eye will bear no relation to the responses to neat shampoos in the rabbit eye. It is really a matter of quantity and not quality.

DR. J. MCL. PHILP: I want to support Dr. Harper in what he has just said. It is most important that you do pay attention to complaints and that you go to quite considerable lengths to have these investigated to make quite sure that your particular product has caused a complaint, and to determine exactly the degree of damage, using an ophthalmologist if necessary. If you set even a few of these accidents against your own predictive testing, then the rabbit eye test can be an extremely useful tool to all marketing and research members of industry.

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(10) Brasch S. V. and Amoore. Miss J. A. *J. Soc. Cosmetic Chemists* **18** 651 (1967).

MRS. S. M. LUDFORD: When I first looked at your paper and glanced down your mean scores in the tables, I came to conclusions about the relative irritancy of these products and was somewhat surprised to find this was very different from your conclusions. When I looked back I found this was due to the maximum persistence in days. The actual scores do not seem very different; in fact shampoo B has, if anything, slightly higher mean scores than shampoo A. Could you comment on the score value? I would have expected a higher mean score value if the persistence was longer.

MR. R. E. DAVIES: I was always taught that you can prove anything with mathematics. The actual scores are relatively unimportant; it is the interpretation of the results and the reactions you observe that are important. The essential facts are that with shampoo B the cornea was not damaged, and therefore we can say that the potential irritancy of this product is considerably less than with the other shampoo formulations. Admittedly there was extensive conjunctival reaction, but the importance of this is dubious in the rabbit, which has well-developed conjunctival structures compared with man and other species. The interpretation of the observed reactions must, therefore, place shampoo B lower on the hazard list than shampoos which irritate the cornea of the eye.

MRS. S. M. LUDFORD: Does this mean that the mean score does not really mean very much; that you should not perhaps take much notice of it?

MR. R. E. DAVIES: Mean scores are of value. If we are comparing two products that affect only the conjuctivae, then a difference in the mean scores is of real meaning. If we are comparing two products, one with a higher conjunctival score but no effect upon the iris and cornea, and the second which has possibly greater penetrating powers and causes extensive corneal damage, but with relatively little effect upon the conjuctivae, I would discard the one that damaged the cornea. The Draize scoring system is, in fact, deliberately weighted to give higher scores for corneal and iridial responses, but there will obviously be instances that are not covered, and this will probably always be so with a mathematical system unless it becomes very elaborate.

MR. W. S. BEACH: In determining whether there is any predictive value to the tests given, you conceded the point that the behaviour of rabbit eyes is not necessarily identical with that of human eyes. You then went on to say that if you use a set of values for one particular substance as basis, you can predict the behaviour in human eyes of another substance based on its behaviour with rabbits. I would like to suggest that this is improbable or of dubious value, because you have no grounds for supposing that because A reacts this way with rabbits and produces a certain reaction in humans, because B reacts this way with rabbits, by comparison with A it is bound to be just as bad with humans.

MR. R. E. DAVIES: I do not use the word "probable", I say "possible". I would like to know the exact formulation of each test material, and eventually we hope to correlate this with the effects upon the eye. Knowledge of the physiological and other differences between the rabbit and human eyes would then permit more realistic interpretations of hazard-in-use. At the present time we are in a very dubious position to do any predictive comparisons. However, we do need a guide line, and it

does seem that the rabbit test can be of value here. With all animal tests we should never be too dogmatic about our assertions as to what effects the product will eventually have in man; he is a different animal species.

MR. A. FOSTER: What exactly did you use as a criterion of choice in the shampoos selected? Was it purely a matter of physical state?

MR. R. E. DAVIES: We accept the advice of the Toxicology Committee of the Society as to the cream shampoos that held the "lion's share" of the commercial market in Britain at that time. The chemical and physical nature was not considered at that time; this was a secondary interest.

MR. A. FOSTER: The decision, then, as to what was a cream shampoo was not yours?

MR. R. E. DAVIES: No.

DR. A. W. MIDDLETON: You have assembled your rating results into what you call mean scores, and therefore, for your mean scores to be any valid measure of the total effect, the differences in the steps of your rating scale must be equal. What steps have you taken to make sure that these are equal? Is the difference between non-irritant and slightly irritant at one step, the same difference as that between moderately irritant and severely irritant?

MR. R. E. DAVIES: In these studies we used standard test procedures which we have quoted at the beginning of our paper. These tests have defined results which are, admittedly, very limited. There is no division into slight, mild, moderate and severe irritants. In the FDA test the product is defined as an "irritant" if it produces a positive test result, and the Draize test defines only "severe irritants". In our study we have interpreted the results as defined in the test procedures.

The classification chart given in the paper is one devised by us in an attempt to categorise products more realistically. It is a purely arbitrary system and is used only as a guideline.

Your comments on mean scores, I think, have already been covered. They are of value in certain situations.

MR. E. A. GOODE: Cream shampoos have now been on the market for many years. I do not know whether some people have suffered damage but has any opinion been expressed in the medical press as to whether there is a severe problem here?

MR. R. E. DAVIES: We do not receive details of consumer complaints routinely and they are not widely publicised possibly because, as Mr. Pugh indicated, they do not exist. It could well be that the users of cream shampoos do not experience ocular irritation. I certainly have not seen the medical profession called in on this.

DR. K. H. HARPER: I just want to make the point that we have used a form of abbreviation in presenting the tables. Mean scores are based on reactions in three different parts of the eye, and I think it is arguable that this is not justified because of the different degree of importance that is attached to the different structures. It would have been more correct for us to have reported mean scores for cornea, iris and conjuctivae separately, but this would have made the tables three times as big, and for this reason we decided to abbreviate. I think it is a very valid criticism that the abbreviation is perhaps misleading in this instance.

ADDENDUM

Since presenting this paper the following physical and chemical characteristics of the samples (*Table VI*) have kindly been studied for us by Mr. N. J. Van Abbé (Beecham Products UK):

a. Chemical composition of detergent ingredients;
b. hydrogen ion concentration (pH), measured by the EIL meter; and
c. viscosity values (centistokes): for shampoos A and B measured by the Brookfield RVT synchro-lectric viscometer, and for shampoos C, D and E by the Ostwald capillary G-tube viscometer.

Table VI

Shampoo code	Detergent ingredient	pH	viscosity cS
A	Sodium lauryl sulphate and sodium stearate	7.9	30,750
B	Monophenylamine and ammonium lauryl sulphates	6.8	4,883
C	Monoethylamine lauryl sulphate and calcium stearate	6.6	1,041
D	Sodium lauryl ether sulphate	6.2	358
E	Sodium lauryl ether sulphate	6.0	1,029

CONCLUSION

No association between any one of these characteristics and the observed irritancy is apparent.

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Contact dermatitis from cosmetics

E. CRONIN*

Presented at the Symposium on "Product Testing", organised by the Society of Cosmetic Chemists of Great Britain in Eastbourne, Sussex, on 15th November 1966.

Synopsis—Allergic reactions to cosmetics are described and the difficulties in technique and interpretation of patch tests are discussed. Lipstick, nail varnish and hair dyes are the most common sensitizers but sensitivity to lanolin also occurs. An unusual urticarial reaction to hair bleach and a phototoxic effect of perfume are described.

In relation to the vast amount of cosmetics used, it is true to say that it is uncommon for cosmetics to cause allergic contact dermatitis. However, from the point of view of a dermatologist, allergy to some types of cosmetics is by no means a rarity. At St. John's Hospital for Diseases of the Skin in London, in the period 1960-1965, we have seen and investigated patients who have developed dermatitis from lipsticks, nail varnish, hair dyes, foundation creams and other types of cold creams and face creams, face powder and mascara.

To establish the diagnosis of an allergic contact dermatitis, patients are investigated by patch testing. Unfortunately, particularly in the hands of the inexperienced, this technique has many pitfalls. Magnusson (1, 2) has shown that both toxic and allergic reactions can be influenced by the type of plaster used and the site of application of the patch test. He found diminished toxic and allergic responses, to a standard amount of chemical, when applied on a patch test in which the size of the lint was comparatively large and it was not isolated from the surrounding adhesive by *Cellophane*. He also found that reaction to a toxic chemical was greater on the upper

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back than on the lower back, upper arm, forearm and thigh. With allergic reactions the variations were less marked but the response was greater on the back than on the arm, and least on the thigh. When patch testing with cosmetics, the cosmetic itself is applied and, if it is known, the ingredient which is likely to be the allergenic component. The tests are removed and read at 48 hr and read again at 96 hr; this latter assessment is important, because it is not unusual for the test to become positive during the second and fourth day. Due to the enhancement of penetration by the closed patch test, a toxic reaction may be produced by an ingredient, which is not an irritant under the conditions of normal use. The appearance of such a toxic reaction may be a typical toxic soap reaction but it can also completely simulate an allergic response. To evaluate a doubtful reaction the open test is used, the preparation being rubbed on to an area of normal skin, usually on the forearm, three times a day for two days and the site is then examined. The preparation is also applied to normal controls. A positive open test is considered to be significant, the cosmetic is fractionated and the patient tested to the ingredients. Tracing the allergenic, or toxic component of a cosmetic can be difficult. The patient may be reluctant to return for tests, which are only of academic interest; it is occasionally difficult to ascertain the composition of a particular preparation or in some instances the patient may react repeatedly to the whole substance but to none of the individual components. Such a reaction has been reported by Rieger and Battista (3), who found that a positive reaction to a preparation could not be traced to a single component but on testing to a combination of the mineral oil and the sodium alkyl sulphate in water a positive reaction was obtained. The mineral oil was changed in the preparation, and no further irritant reactions occurred.

Lipstick is the commonest cause of cosmetic dermatitis and may be diagnosed by the patient herself with some certainty. During the past six years, 38 patients have been seen with dermatitis of the lips due to sensitivity to eosin. Their ages ranged from 21-75 years; occasionally the patient relates the swelling and soreness of her lips to the buying of a new lipstick but in general the condition develops for no obvious reason. Sulzberger *et al* (4) reported that it was the halogenated fluoresceins which are the usual sensitizers in lipsticks, and Calnan (5) confirmed their findings that the allergen is an impurity in eosin which can be removed by repeated crystallization. Patch testing with the patient's lipstick is unreliable for the detection of eosin sensitivity. Eosin binds with keratin and the amount present in an ordinary lipstick is too small to saturate the keratin and allow

eosin to penetrate through the horny layer. This is overcome by increasing the concentration of eosin to 50% in a standard lipstick base or in *Vaseline*, and by rubbing the lipstick or eosin stick directly on to the skin, thus ensuring that an adequate amount is applied. Patch testing of the patient's lipsticks is always done to detect sensitivity to a component of the lipstick other than eosin. It is noticeable that the incidence of lipstick dermatitis is decreasing; whereas 29 patients were seen during the three years 1960–1962, only nine patients were seen in the years 1963–1965. This is probably a reflection of the gradual replacement of the halogenated fluoresceins. Wilmsmann (6) has reported the successful use, in lipsticks, of the FDC & DC azo dyes in the form of free sulphonic acids; in this form, these dyes stain the lips and give a better range of colours than the eosins.

During this period five patients were seen and found to react to components of their lipstick other than eosin. In two, the allergen was the lake D & C Red No. 31 (calcium salt of 3-hydroxy-4-phenylazo-2-naphthoic acid); one of these was also sensitive to D & C Red No. 19 (3 ethochloride of 9-*o*-carboxyphenyl-6-diethylamino-3-ethyl-imino-3-*iso*xanthine). A third patient, reported by Calnan (7), was sensitive to the barium lake of D & C Orange No. 17 1-(2,4,dinitrophenylazo)-2-naphthol, and a fourth to the perfume in a lipstick. The fifth patient did not re-attend for further investigation. In 1961 a patient was seen who, knowing that she was sensitive to ordinary lipsticks, tried to use a "barrier" lipstick and developed soreness of the lips. On patch testing she reacted to the barrier lipstick and on testing to its components was found to be acutely sensitive to azulene (cyclopentacycloheptene). The azulene was presumably incorporated as an anti-irritant.

Allergy to the aryl sulphonamide formaldehyde resin in nail varnish is the next most frequent type of cosmetic dermatitis that occurs. In this six year period, 33 patients were seen, their ages ranging from a girl of 15 years to a woman of 67 years. The face and sides of the neck are practically always the site of the dermatitis, in particular the eyes are often red and itchy. The nail beds are not affected because, in general, the nail-plates are impermeable to the lacquer. Patients are tested to their nail varnish, which is allowed to dry on pieces of lint before being applied to the skin, and they are also tested to the aryl sulphonamide formaldehyde resin, 10% in *Vaseline*. As the dermatitis is so remote from the responsible nail varnish, this condition can easily be missed if the clinician is unaware of the pattern of dermatitis which nail varnish causes. Patients never suspect their varnish and may be frankly sceptical of the possibility until proven

by patch testing and the healing of their rash on discontinuing to wear nail polish. In contrast to the clinical findings in these patients, Rein and Rogin (8), from the United States, have reported 47 patients who developed discoloration, separation and the accumulation of debris under the nail plates after using a base coat. This base coat contained a phenol formaldehyde resin; of the 32 patients tested to it 27 were found to be positive. They thought the resin actually penetrated the nail plate rather than the nail bed being contaminated during manicuring. A similar picture of inflammation of the nail bed, due to a base coat, has been reported by Reisch (9). In this instance the patient was not sensitive to the lacquer nor to its ingredients.

An allergic reaction to hair dye is rarely missed by either patient or the physician. This allergy is widely known, by both the public and their doctors and is not so commonly seen by the dermatologist. 23 patients have been investigated in the past six years. It is likely that this number does not reflect the true incidence of the condition as many patients are probably diagnosed and treated by their own general practitioners, without reference to hospital. An allergic reaction to hair dye may begin within hours and is usually fully established within one or two days. The reaction tends to be acute and severe, with weeping of the scalp, redness and swelling of the face. The eyelids become puffy and swollen and the eyes may be completely closed, so that the patient is temporarily blinded. Patch testing should be deferred until the dermatitis is healed. This is necessary to avoid (a) a false positive reaction due to the irritable state of the skin in the acute stage, and (b) a false negative result, because in the acute phase the patient may temporarily be unable to react to the allergen and also to avoid a flare of the dermatitis secondary to a severe reaction at a patch test site. When recovered, the patient is tested to *p*-phenylenediamine 0.5%, *p*-toluylene diamine 1%, and *o*-nitro-*p*-phenylenediamine 2%. This is one of the few types of cosmetic dermatitis that afflicts men as well as women; of the 23 patients referred to above, three were men, of whom two were either Indian or Pakistani.

A most unusual reaction to hair bleach was described by Calnan and Shuster (10). A few patients were seen who, immediately after the application of bleach to hair, developed tingling of the scalp, redness and swelling of the face and in a severe reaction lost consciousness. Similarly, a hairdresser described irritation of her scalp or hands after contact with bleach. The reaction was found to be caused by ammonium persulphate. A saturated solution of ammonium persulphate applied to intact or scratched skin

caused the development of an urticarial wheal. The wheal took minutes to develop and could not be elicited in skin depleted of histamine. 57 normal controls were tested and of these, four developed small wheals, and three developed large wheals. In the patients investigated, no definite conclusion was reached as to whether the reaction was an allergic immediate type antigen-antibody reaction or whether it was a direct release of histamine in a susceptible individual.

Perfumes may cause allergic contact dermatitis. The reaction may be due to a perfume used as such or as an ingredient in an other cosmetic. Perfumes are alcoholic solutions and must therefore be diluted to 2% in olive oil for patch testing. A positive open test, in which the pure perfume is applied directly to the skin, is good confirmatory evidence of sensitivity. Identifying the allergen is difficult or completely impossible because of the complex nature of one perfume. It sometimes happens that after the application of a perfume and subsequent exposure to sunlight, brown pigmentation develops at the sites where perfume was present on the skin. This is known as berloque dermatitis (berlocke = pendant) because of the patterning of the pigmentation, which may resemble a hanging drop – particularly on the neck, where the perfume has trickled from behind the ear. The mechanism is not allergic but a photosensitivity due to the presence of phototoxic chemicals, probably psoralens, in the perfume. It is a difficult reaction to reproduce but Haber (11) succeeded by applying the perfume under polythene, thus enhancing its absorption. Subsequent exposure to sunlight, directly and through window glass, caused the development of erythema.

Face creams and foundation creams cause little trouble, only eight patients having been diagnosed as being allergic to a preparation of this type. In five the allergen was traced. In three it was lanolin, in one the perfume, and in the fifth beeswax in a cold cream. Lanolin dermatitis, although uncommon, does occur (12), and all patients suspected of having cosmetic dermatitis are now routinely tested with 30% wool alcohols in *Vaseline*. This high concentration is used because sensitivity to lanolin is difficult to detect by patch testing; the reason for this may be that the allergen is poorly absorbed or that it is present in minute amounts or because it is a weak antigen. Patients with cosmetic dermatitis due to lanolin in a cream preparation are positive on patch testing to the cream itself, and to 30% wool alcohols in soft paraffin. The presence of lanolin in the cosmetic can be confirmed from the manufacturers, and the patient is given a list of cosmetics not containing lanolin, which may be used safely.

Face powder rarely causes dermatitis; only three patients were seen who gave a positive patch test to their face powder, but in none was the allergen traced. A fourth patient was found to be sensitive to lanolin, a small amount of which was present in the pancake powder she was using. On changing to loose powder all the symptoms subsided.

Mascara, eyeshadow and eye-liners are frequently thought by the patient to be the cause of irritation, redness and swelling of the eyelids. It is possible that these cosmetics, in particular mascara and eye-liner, may sometimes act as mild irritants and the patient may be intolerant of them. On patch testing, however, it is rare for an allergic sensitivity to be found. Three patients were thought to be sensitive to mascara, in two the component fractions were tested. In one, they were all negative and the mascara test also became negative. The other patient reacted to a test mixture of undecylinic acid and beeswax; unfortunately she refused to return for further patch testing and which of these two caused the reaction was not determined. Epstein (13) has emphasised that under an occlusive patch test mascara, particularly some of the liquid forms, frequently gives a false positive reaction, which may be indistinguishable from an allergic response. He attributed this effect to the presence of solvents and found that it could be avoided by using a non-occlusive patch test, in which the mascara was covered by a freely permeable dressing.

Eye-shadow seems to be innocuous, and we have not had a patient with a proven sensitivity to this cosmetic.

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Introduction by the lecturer

Recently we have investigated patients with lanolin sensitivity which is difficult to detect. We have found that the best method of patch testing is to use 30% wool alcohols in *Vaseline* or Ung. Aquosum, B.P. which contains 3% wool alcohols, and apply it to the skin under polythene. The latter method is effective but when the reaction is positive the test unfortunately causes rather a large patch of eczema. While investigating these patients with lanolin sensitivity we attempted to identify the actual allergen in the wool alcohols. Fractions of the alcohols were obtained by crystallisation and patients were patch-tested, but there was no uniformity of results. The response varied from patient to patient and it seems definite that there is more than one allergen responsible for lanolin sensitivity; this would account for the fact that lanolin-sensitive patients can sometimes tolerate one lanolin preparation but not another.

DISCUSSION

Dr. K. Sames: I consider that over-due importance is still being attributed to the effects of eosin as such, in particular, and to the other halogenated fluoresceins as such, in instances of lipstick dermatitis. I am sure that it is agreed from all sides that the actual number of instances of lipstick dermatitis has decreased appreciably over the last few years to such proportions that it is now practically negligible. In an attempt to study to what extent eosin or any particular halogenated fluorescein is the kingpin of lipstick dermatitis complaints, I have made a study of all the customer medical complaints of lipsticks received by my own company over the period 1962-65 inclusive. I must emphasise that the total number received is so small as to be mathematically insignificant by comparison with the very large number of lipsticks sold over the open counter, and that I have not been able to follow up individually even this small number so as to be able to ascertain whether they were genuine medical complaints or not. I have, therefore, accepted each one of these complaints for the purpose of this study as though it were unqualifiably genuine and have studied the formulations of the various shades of lipsticks involved only on the basis of the halogenated fluoresceins contained therein, since the base and perfume and other raw materials are in the main common to all the formulations.

The units, in which I have shown in *Table I* the frequency of occurrence, have no denomination whatsoever because they represent so very small a number averaged over four years and have then been averaged over the number of shades which actually contain the particular pigments which have been typified. They can, therefore, only be taken as a ratio figure and without any true numerical value. *Table I* indicates that there are nine groups which in actual fact represent 21 shades of lipsticks and that these nine groups subdivide themselves into five of very small numerical units, two of very slightly greater intermediate arithmetical value of units and two of appreciably higher number of units, approximately six times as great as those of the lowest group. I am not attempting to postulate any significance here but the following apparent hypotheses emerge:–

1. The presence of tetrabromo alone gives no greater incidence figure than if none of the halogenated fluoresceins are present, and the same applies when dibromo is used alone or when dibromo is used with tetrachlorotetrabromo or when di-iodo is used with tetrachlorotetrabromo. The middle group, approximately two and a half times

Table I

Halogenated fluoresceins in the various shades of lipsticks, either as such or as natural commercial lakes.	Average incidence of medical complaints expressed as a mean over the number of shades of lipsticks involved per year over the four years.	Group of sub-divisions:– A = Smallest no. of incidences B = Intermediate no. of incidences C = Largest no. of incidences
None.	1.25	A
Dibromo alone.	1.25	A
Dibromo plus tetrachlorotetrabromo.	0.50	A
Di-iodo alone.	2.50	B
Di-iodo plus tetrachlorotetrabromo.	0.25	A
Di-iodo and tetrabromo.	5.50	C
Di-iodo plus tetrabromo plus tetrachlorotetrabromo.	6.90	C
Tetrabromo alone.	1.30	A
Tetrabromo plus tetrachlorotetrabromo.	2.90	B

as high in value as the lower group, is when di-iodo is used alone or when tetrabromo is used with tetrachlorotetrabromo. The highest group did reveal appreciably higher figures although it must be emphasised that the actual number of complaints is still extremely small. It comprises the two sets of circumstances in which di-iodo was used with tetrabromo and when di-iodo was used with tetrabromo and tetrachlorotetrabromo. The significance here probably is that in both these groups di-iodo is used with tetrabromo. To all intents and purposes the same quality, probably even the same batches of tetrabromo and di-iodo were used in all cases and yet, for what the figures are worth, when the di-iodo is mixed with the tetrabromo, there result appreciably higher figures than when the di-iodo is used alone or when the tetrabromo is used alone. The actual degree of purity of the batches of pigments, originally my main line of thought, appears to be of only debatable value in view of this frequency.

2. Since the values found when none of the halogenated fluoresceins was involved are to all intents and purposes identical with those found when eosin alone is involved, and in view of the desirability not to give detractors of our industry a false opening gambit to their campaigns, I would strongly urge that the association of the word eosin with hypersensitivity in cosmetics application should be actively discouraged, since we must accept, and I am sure you will agree, that almost any material could, if the patient were ripe for it, induce hypersensitivity in the area in which it is applied.

THE LECTURER: We have only seen about nine cases of sensitivity to eosin in the past three years, whereas in the previous three years we saw approximately 30; thus previously there were about ten a year as compared to about three a year now.

DR. K. SAMES: Do you have any views on the greater number of instances of sensitisation due to barium lakes by comparison with those of aluminium and titanium?

THE LECTURER: No.

DR. K. SAMES: There are available on the market qualities of titanium dioxide which assay 99.0%+ TiO_2 and others which assay 98.5%+ TiO_2. The differences would appear to be fundamentally insoluble trace impurities and variations in moisture. Dealing only with the trace impurities do you have any views on hypersensitisation or primary irritation induced by trace impurities in commercially available grades of titanium dioxide?

THE LECTURER: We have never seen sensitivity to titanium dioxide.

DR. K. SAMES : I believe you to be aware of one instance of proven hypersensitisation to uv light absorber, which I made privately to Prof. Calnan recently. Do have you any information and views on hypersensitisation induced by these agents in general?

THE LECTURER: The only uv light absorbers we see occasional sensitivity to are the benzophenones used in ointments for photosensitive patients. We also see sensitivity to *p*-aminabenzoic acid.

MR. C. PUGH: Dermatologists have quite a problem with a patient, in tracking down the cause of the reaction. Product developers have perhaps even more difficult a problem when they are to use new materials, and they must use new materials if they are to maintain progress. If one is diligent and does, say, 1000 patch tests on a new product and nothing at all happens, statistics will show that you have the probability of not more than 1 in 3000 of the public reacting to your product. This is not a very acceptable risk to a manufacturer. If 1 in 100,000 react, one would be somewhat worried when a product sold on a national scale by the millions. Most firms overcome this with an entirely new product or material, by test-marketing first and gradually expanding their market. Can you offer us a better way of finding out how safe we are before we go into the market, and do you have any views on the ethics of greatly expanding test markets, in lieu of any other way of assessing safety?

THE LECTURER: I have nothing to offer. I do not know how you would detect the odd individual who will react – the 1 in 3000 or 10,000. It would be chance if they turned up in a small series, and as far as ethics are concerned, I see no reason why one should not run a pilot trial in a small community. I suppose with any new product, or any new constituent, you are likely to find somebody who will react to it, and I do not know how you can guard against this.

MR. N. F. E. BLACKMORE: Is there any evidence that if a person is sensitive to one chemical, say *p*-aminobenzoic acid, that person is more sensitive to other chemicals that may cause reactions in other people? Perhaps one could construct a panel of highly sensitive people?

THE LECTURER: There is some evidence to suggest that a person sensitive to one substance is more likely to develop sensitivity to another. I think a panel of people sensitised to many substances would give misleading results. The other point to determine is whether the reaction of 1 in 3000 is a primary irritant or a sensitivity response.

MR. A. HERZKA: Does the clinical state of a person alter the sensitivity, i.e. is a nervous person more sensitive to chemicals than a placid one?

THE LECTURER: I would say this has no effect.

MR. A. M. NETHERWOOD: You have remarked upon the reactions which have been caused by plasters during patch testing. There has now been available on the British market for some considerable time a plaster which has a single component adhesive base and this produces far less reactions than the usual resin-rubber. This is very good for applying patch tests.

THE LECTURER: A porous or a non-porous tape?

MR. A. H. NETHERWOOD: It is less porous than the perforated tapes but more porous than the straight plastic film-covered tapes.

MR. J. McL.PHILP: You have been very clear indeed about the pitfalls of the diagnostic patch test, and I understand that there has been an attempt to overcome some of the pitfalls, notably in Scandinavia, where collaboration between five dermatologists has resulted in a very standard patch test. Do you see any possibility for a similar collaborative effort in this country, and do you consider that there is need for such collaborative work?

THE LECTURER: There is a great need for the standardisation of patch testing. If the same sites, same bases and same tapes were used by all investigators, it would give a much more valid comparison of results.

MR. N. J. VAN ABBÉ: Under the auspices of the Society we have been carrying out a collaborative patch test with about eight different laboratories, including a dermatologist and some other medical collaborators. The results are currently being analysed with a view to publication in the *Journal*. This is, of course, a prophetic patch test scheme for primary irritants and we have not been attempting diagnostic patch tests for allergens, which I personally regard as the province of the dermatologist. Nevertheless, we do seem to have obtained some very interesting results in this collaborative study and look forward to publishing them very soon.

MR. C. PUGH: Is the incidence of primary irritations more prevalent in the summer than in the winter?

THE LECTURER: I do not think this is really known. This question is often raised, but clinically we do not notice a seasonal variation. Theoretically, increased sweating in the summer, with hydration of the stratum corneum, should facilitate penetration of chemicals, so that the incidence of sensitivity might be expected to rise. If such a difference does exist it would need a very detailed study to detect it.

MR. N. J. VAN ABBÉ: Do you really think that berloque dermatitis is something that deserves a clinical description? Are the reactions which are diagnosed as berloque dermatitis anything to worry about?

THE LECTURER: They are nothing to be worried about; this is a very distinctive clinical picture of patterned brown patches, usually on the neck, where the perfume has trickled down. The appearance simulating a pendant or hanging drop has given the condition its name. It does not mean that the next time a perfume is put on the condition will recur. The persons are not allergically sensitive to the perfume.

MR. D. E. BUTTERFIELD: How frequently do you see this? I once knew, for example, a Hungarian girl who tried to use bergamot regularly for acquiring a tan.

THE LECTURER: It is not a very common condition but one that is easily recognised. I do not have any figures on the exact incidence.

DR. K. SAMES: You attribute berloque dermatitis to the presence of phototoxic chemicals, probably psoralens in the perfume. The authors of the older textbooks used to attribute berloque dermatitis to the presence of traces of copper in the oil of bergamot employed in the perfumes, picked up either during distillation in copper plant or through transport in copper containers (always referred to in the trade as "coppers" irrespective of whether they are made of the metal or not). Indeed it is believed that considerable alterations to the distillation process, and certainly the tinning of coppers and their subsequent replacement by tinplate, were influenced by this traditional belief and the effects of these traces of copper derivatives through the use of perfumes in which bergamot was employed. Would you say that this theory is now obsolete in view of your remarks regarding phototoxic chemicals?

THE LECTURER: I did not know that copper had been thought to be the cause. It is the furocoumarin in the perfume which causes this photosensitivity.

MR. D. E. BUTTERFIELD: Have you tried rectified bergomet?

THE LECTURER: Trying to reproduce a berloque dermatitis experimentally is difficult. I have only seen this reaction reproduced in a patient who rubbed a rue leaf on her arm, went out into the sun and developed a marked erythema at the site. Haber (11) reproduced berloque dermatitis by applying the perfume under an occlusive dressing and produced an erythema on exposing the site to sunlight.

MR. A. FOSTER: One often gets a query from the public — do your cosmetics contain Orris? Frequently the writer states "my doctor suggests that it might contain Orris". Can you throw any light on this perpetual query? We know it is a known allergen but has any work been carried out on determining the presence of Orris, and its present-day importance?

THE LECTURER: I was under the impression that it was not used today. I think the statement that Orris can be dangerous just gets handed on from one person to another but I have never seen any reaction to it, and never known it to be used.

MR. A. FOSTER: This is precisely the point I wish to make; it is time that this bogey be abolished.

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Letter to editor

12th July 1967

THE SEPARATION OF NITRO-DYES BY ELECTROPHORESIS

In the discussion of a recent paper in the *Journal* (1), one of us reported that our experience had shown that electrophoresis was the only satisfactory method of separating the isomeric nitrophenylenediamine dyes. Brown's *Fig. 1* (1) shows the typical failure of paper chromatography to accomplish this separation.

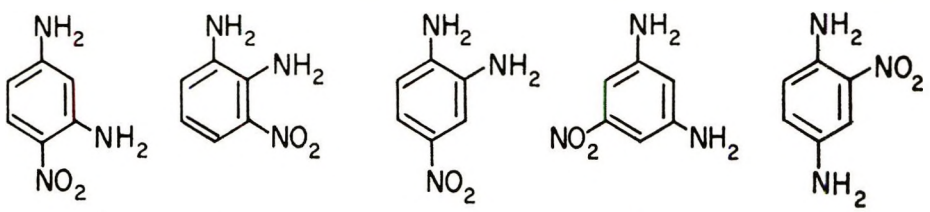
Our electrophoretic technique employs 1 M aqueous acetic acid as the electrolyte and either Whatman No. 1 paper or Gelman Sepraphore III gel strips as the support. Separations can conveniently be performed on a 15-20 cm strip with an applied potential of 10-50 volts/cm.

Table I

Electrophoretic separation of nitrophenylenediamines on a Sepraphor III gel strip for 45 min under a potential gradient of 10 volts cm^{-1} using 1 M acetic acid as the solvent.

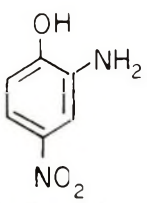
Dye	I	II	III	IV	V
Distance travelled (mm)	0	13	18	35	85

Using this technique, an excellent separation of the five known nitrophenylenediamines (I-V) can be achieved as can be seen from *Table I*. Very sharp bands are produced and those due to *II* and *III* are completely separable under the conditions employed. In the initially developed electrophoretogram all the bands are yellow but, on exposure to ammonia, that due to *V* changes to brick red and that due to *II*

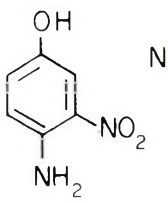


I II III IV V

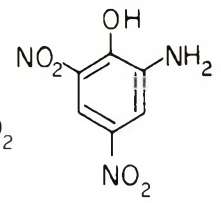
changes to orange. It will be noted that under the conditions employed the dyes migrate as their protonated species and it is of interest to note that the failure of dye *I* to migrate is due to the fact that it is not protonated in 1 M acetic acid—due undoubtedly to the fact that, unlike the other four isomers, this dye has no amino-group *meta* to the nitro-group. For this reason also, the technique is suitable for the separation of *m*-nitroaniline from its isomers.



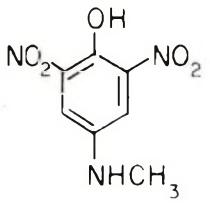
VI



VII



VIII



IX

Other nitro-dyes which are commonly employed in hair colour products are the nitroaminophenols (*VI-IX*). Of these, only compound *VI* migrates under the conditions described above. The remainder are conveniently separated by chromatographic techniques.

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Book reviews

GAS CHROMATOGRAPHY 1966. Editor: A. B. Littlewood. Pp. xii + 464 + Ill. (1966). *Institute of Petroleum, London.* 100s.

This is a record of the proceedings of the Sixth Biennial International Symposium on Gas Chromatography and Associated Techniques organised by the Gas Chromatography Discussion Group, and held in Rome in September 1966.

Gas chromatography is by now a mature, widely applicable but highly specialised technique. These proceedings rightly highlight selected recent advances and the appeal of the volume is therefore mainly to the specialist analyst and physical chemist rather than the more general reader seeking an up-to-date balanced account of gas chromatography.

The main part of the book consists of the 25 formal papers that were presented, each with a summary. By now much of the material has appeared elsewhere in the literature but the book is justified by its collection together in one place of much valuable information and by the often revealing discussion that follows each paper.

Gas chromatography has for long drawn heavily on established physico-chemical theory. It may now repay the debt by providing data for the physical chemist judging by three papers dealing with its application to studies on chemical equilibria, thermodynamics of dilute solutions and hydrogen bond energies.

Two new types of stationary phase are discussed. Graphitized thermal carbon black retains molecules largely in accordance with their planarity and can give some remarkable separations of terpenes. The well publicised microporous polymers yield some novel separations particularly of polar compounds.

Two papers deal with improving column performance. Glass capillary columns are treated in one and liquid chromatographic columns in the other. The latter, envisaging separations comparable in speed and resolving power to gas chromatography, is particularly relevant with recent innovations in liquid chromatographic detectors.

Preparative glc is usually a batchwise process. Two contrasting practical designs of circular gas chromatograph demonstrate the possibility of a continuous separation.

Three detectors are detailed. A modified flame-ionisation detector is specific for organosilicon compounds and a coupled flame-ionisation/sodium thermionic detector is specific for compounds containing halogen or phosphorus. The third detector, termed a reaction coulometer, works on a "feed-back" principle and claims calculable responses amongst its advantages.

Probably the most significant amongst a group of papers on novel applications is one showing that the direct resolution of optical isomers on an optically active liquid phase need not be just a tantalising dream—excellent separations of pairs of enantiomers of certain amino acid derivatives were achieved. Another paper shows how this type of problem can be solved through conversion to diastereoisomers. Evaluation of heterocyclic nitrogen compounds in atmospheric dusts, ultra-trace

analysis of beryllium (down to 4×10^{-13} g) and analysis of metal chlorides are the remaining papers in this group—a group indicating the wide range of gas chromatography when imaginatively applied.

No technique is complete in itself. The direct coupling of a mass spectrometer to the exit of a gas chromatograph produces an analytical tool of immense power and this is duly treated in this volume. However, for most of us, this combination is on the wrong side of a financial barrier and the description of an apparatus that combines relatively cheap mass and ir spectrometers with glc by modifying the chromatographic technique ("interrupted elution") will be of more immediate interest. The use of digital computers to treat complex chromatographic data is exemplified in two papers. Isotope dilution techniques are shown to improve the accuracy of analysis of trace components and a type of zone refining in reverse is detailed as an excellent concentration procedure for volatile flavour compounds in dilute aqueous solution.

The last formal paper presents the results of an interlaboratory correlation trial using a fatty acid ester/hydrocarbon mixture. It provides a salutary reminder after all that has gone before that some of the "simple" gas chromatographic problems have not yet been fully solved.

The ten informal discussion sessions on topics ranging from commercial instruments to flavours and essential oils are reported in 39 pages and will repay a close and critical study.

A list of delegates and good indexes complete a well-produced volume.

R. N. BEVITT

GAS CHROMATOGRAPHY ABSTRACTS – 1966. Editor: C. E. H. Knapman. Pp. xi + 315 (1967). *Institute of Petroleum.* 63s.

This hardy annual is welcome by all involved with gas chromatography, even those who have found it advantageous to join the Gas Chromatography Discussion Group of the Institute of Petroleum and receive the abstracts quarterly, and subsequently the annual volume at a reduced price.

This is the ninth volume in the series and contains 1200 references (i.e. the contents of the four quarterly instalments published in 1966) abstracted from a wide and comprehensive selection of journals.

There has been a slight revision of subject index headings which is clearly explained under the heading of "Principles of Indexing" and this successfully aims to give a maximum number of cross references. The volumes of cumulative Indices for 1958-1963 inclusive is now available. Tables of retention indices of solutes on squalene, dinonylphthalate and polyethylene glycol 400 are included for the first time. These tables are produced by the Data Subcommittee of Gas Chromatography and are a useful addition.

Another new item is a trade name glossary of gas chromatographic materials and their chemical equivalents.The list is not exhaustive but it will be extended in due course and readers are asked to contribute where possible. In common with all abstracts there is an inevitable time delay but this volume is a very useful addition to every gas chromatographer's reference library. Its best features lie in its compact size, comprehensive cover of published work and an effective indexing system.

Mrs. D. M. GABRIEL

QUANTUM ORGANIC CHEMISTRY.

K. Higasi, H. Baba, A. Rembaum. Pp. vii + 358 + Ill. (1965). *John Wiley & Sons, New York, London, Sydney.* 98s.

'Quantum Organic Chemistry' first appeared in a Japanese edition in 1956. Since then the original authors, in collaboration with Dr. Rembaum at CalTech, have rewritten some of the introductory material on molecular orbital methodology and have considerably expanded the treatment of the applications of quantum mechanics to organic chemistry, notably chapters dealing with dipole moments, electron spin resonance, polymerisation reactions and chemical reactivity. Every chapter, theory and practice, is supplemented by a concisely worded summary of salient features presented.

Of particular interest are the 40 pages examining, on an MO basis, the electronic transitions involved in molecular absorption spectra. This is a good introductory account for the organic diagnostician with an interest in rationalising his spectra without wishing to set up a research project in the theoretical hinterland between chemistry and physics. The purist might cavil at the occasional solecism, e.g. the indiscriminate use of 'red shift' and, more nonsensically, 'blue shift' for (respectively) bathochromic and hypsochromic effects entirely in the uv regions of the absorption spectrum. With more justification one objects to superficialities such as the alleged "consideration" of the effect of electron withdrawing groups on π—π^* transitions which in fact consists of only a few chatty lines.

But these are minor blemishes in a book that undoubtedly supplies a genuinely readable exposition of the applications of MO theory with only the necessary minimum of fundamentals virtually uncluttered with the esoteric mathematics that often bedevils organically biased students or may deter them after graduation.

G. F. PHILLIPS

TECHNIQUES IN PROTEIN BIOSYNTHESIS. Vol. 1.

Editors: P. N. Campbell and J. R. Sargent. Pp. xii + 336 + Ill. *Academic Press, London/New York.* 80s. $15.00

Understanding of the mechanism of synthesis of proteins in living tissues has advanced so rapidly that it is surprising to realise that as recently as 1953 theories involving peptide intermediates and classical enzyme reactions were still in vogue. These theories were already proving their impracticability, however, when the crucial experiments demonstrating the template mechanism of protein synthesis were carried out. Since then the mechanism of the process has been worked out in considerable detail. It is the object of this book to describe the techniques which have been used in this field of research. and it is primarily aimed at new entrants to the field.

A general review of the field is provided by the editors in an introduction covering 63 pages. This review deals with the historical development of current theories; with the system of coding carried by the base triplets making up the nucleic acid chains; with the mechanism of transfer of this information from DNA in the nucleus to messenger RNA which goes to the ribosomes; with the method of activation of individual amino acids, and their attachment to their specific soluble (transfer) RNA'S;

and the final linking of the amino acids at the ribosomal sites according to the coding contained in the messenger RNA. A further section correlates the morphology of the cell with the process of protein synthesis.

Other chapters, which are also contributed by authors who are active workers in the field, are concerned mainly with the techniques used. A. von der Decken ("Methodological aspects of protein synthesis in mammalian systems") deals with the radioactive techniques involved in the incorporation of labelled amino acids into proteins both *in vivo* and *in vitro*, and the determination of radioactivity in proteins. J. R. Sargent ("Biosynthesis of specific proteins in mammalian systems") discusses the techniques which have been used in studies of the biosynthesis of haemoglobin and of proteins in liver, mammary gland, pancreas and oviduct. M. S. Bretscher and O. W. Jones ("The biochemistry of the genetic code") deal with the techniques used to correlate specific amino acids with specific base triplets. And K. S. Kirby ("Isolation of ribonucleic acids for studies in protein biosynthesis") writes about transfer RNA, ribosomal RNA, and messenger RNA. Finally, various general techniques are given in a brief appendix.

This book is aimed primarily at the intending specialist, but the lengthy introduction provides a useful review for the general reader. B. G. OVERELL

THE PALLADIUM HYDROGEN SYSTEM. F. A. Lewis Pp. xii + 178 + Ill. (1967). *Academic Press, London/New York.* 45s. $9.00

As the author states in the preface the palladium-hydrogen system has been perhaps the most extensively experimentally investigated metal-gas system. It is of considerable interest both from the practical and the theoretical standpoint. Probably we are all familiar with the use of palladium as an hydrogenation catalyst but less familiar with its other uses such as a diffusion membrane and in the separation of hydrogen isotopes.

This book is a concise and thorough review of all the work on the palladium-hydrogen system and includes work published as recently as 1966. The usual high production standard of Academic Press is attained and the book includes a comprehensive subject index and a combined reference and author index. For those with an especial interest in this subject this should prove a valuable source book.

R. P. REEVES

Society of Cosmetic Chemists of Great Britain

1967 DIPLOMA EXAMINATION

Borough Polytechnic

PAPER I

(Monday, 19th June 1967)

Candidates should answer FIVE questions from *not less than FOUR* sections.

SECTION A

1. Outline the main functions of a shampoo. Describe the steps you would take in the laboratory to ensure that a detergent was suitable for inclusion in a shampoo. Give a typical formulation for a clear liquid cosmetic shampoo showing clearly the function of the main components.
2. Describe in detail the structure of the hair with particular reference to its chemical constitution.

SECTION B

3. Give an account of the various types of mascara. In each case, discuss the formulation of the product, listing the ingredients used and, if possible, give a typical formula.
   Finally, give an evaluation of the advantages and disadvantages in use of each type of mascara.
4. Give an account of modern lipstick manufacture, paying particular attention to the following points:
   (a) Incorporation of colours into the base
   (b) Colour correction
   (c) Moulding and flaming
   (d) Quality control

Section C

5. Describe in general terms how an aerosol hairspray works. Indicate what changes in the product would affect the type of spray produced and describe how you would improve a product giving a very coarse, wet spray.
6. A handcream is to be packed in a polythene tube. Describe what tests you would do in order to choose between two alternative external lacquers that have been suggested as a coating for the tubes. Also describe briefly how you would determine the approximate shelf life of the chosen pack.

Section D

7. Give an account of the chemical methods of controlling micro organisms used in the disinfectant industry. How would you assess the efficiency of a named germicide under laboratory conditions?
8. Write descriptive notes on four of the following:
   (a) Bacterial cell
   (b) Dematophytes
   (c) Antibiotics
   (d) Q.A.C.'s
   (e) Lysozyme
   (f) Fungicides
   (g) Gram stain
   (h) Ecology of yeasts

Section E

9. Describe in detail, using appropriate diagrams, the structure of a normal human tooth. Define dental caries and outline its mechanism giving as much supporting evidence as you can.
10. What are the main types of shaving product? Describe the different types giving a typical formulation for each and considering the functional differences between them. List, in order of importance, the properties you consider the 'ideal' shaving product should have.

Paper II

(Wednesday, 21st June 1967)

Candidates should answer FIVE questions from *not less than FOUR* sections.

Section A

1. (i) Give one example (chemical formula and name) of each of the following types of detergent—nonionic, cationic and ampholytic.

Using your chosen example, clearly distinguish between these detergent types.

(ii) Describe briefly the industrial process for the manufacture of two of the following types of detergent:

(a) soaps
(b) alkyl sulphates
(c) alkyl ether sulphates

Particular attention should be given to the chemical reactions involved.

2. What is meant by the terms "micelle" and "critical micelle concentration"?

Describe a method for measuring the critical micelle concentration of a detergent.

If the micellular molecular weight of potassium oleate is 29,000 and that of sodium lauryl sulphate is 24,000, how many molecules of each detergent are there in a micelle?

C=12, H=1. Na=23, S=32, O=16

Section B

3. Indicate the chemical nature of the various types of materials with waxy properties which are used in the cosmetic industry and outline their uses. What raw material quality control tests would you apply to each type of waxy material?

4. Describe in as great detail as you can the composition of animal fats and vegetable oils. Explain how and why the chemical structure of these compounds influences their physical properties and their tendency to develop rancidity.

Section C

5. Define the Beer-Lambert law and explain with the aid of diagrams the essential features of a simple spectrophotometer. A 3.3% solution of substance "A" contained in a 0.5 mm thick cell absorbs 72% of light of wavelength λ_A (where substance "B" does not absorb appreciably). A 5.1% solution of substance 'B' in a 0.25 mm thick cell absorbs 41% of light of wavelength λ_B (where "A" does not absorb). The ratio of the optical densities at λ_A and λ_B in a solution of a mixture of "A" and "B" only was 3.7:1. Calculate the composition of the mixture of "A" and "B" (Log tables are provided).

6. Discuss the relative merits and limitations of paper, thin-layer, and gas-liquid chromatography for the analysis of cosmetic products. Describe in general terms the apparatus used for gas chromatography.

Section D

7. What do you understand by the word "perfume"? The following are terms used by perfumers to describe odours. Name for each term one perfumery material which could be so described:— woody, citrus, spicy, animal, floral, balsamic, herbal. Discuss the problems involved in the perfuming of *two* of the following products:

   (a) talc
   (b) lipstick
   (c) white toilet soap
   (d) aerosols

   Discuss how you would test the suitability of a perfume for one of these products.

8. What methods are used for the production of natural products used in perfumery? By which method is (1) bergamot oil, (2) jasmin absolute, (3) lavender oil obtained?
   Write brief notes on the fields of chemistry associated with the natural odorous products used in perfumery.
   Give examples of two chemicals of each field and the products in which they occur naturally.

Section E

9. Explain how emulsifying agents facilitate the formation of an emulsion and how they influence the nature of the emulsion. What other factors influence the nature of the emulsion? Name the different types of amphipathic emulsifying agent and give an example of each type.

10. State Poiseuille's law and indicate under what conditions it applies.
    A given volume of water flows through a capillary viscometer in 45 seconds and an equal volume of an aqueous glycerol solution whose density is 1.12 g/cm requires exactly 11.5 minutes to flow through. Calculate the absolute viscosity of the glycerol solution. (Assume that the viscosity of water is 1.000 cP under the conditions of the experiment and that its density is 1.00 g/cm.[3])

Successful candidates

Eleven out of nineteen candidates were successful. Diplomas were awarded to the following:

Dr. G. Bayraktar	*J. Gokhale	J. A. Rattan
M. T. Chobe	T. G. Hartin	Mrs. S. Sen
Miss E. R. Cohen	I. A. Pannell	J. Woo
G. L. Gangaramani	A. Palkar	

*Hibbott Memorial Prize

1967-68 PROGRAMME

Lectures will be delivered on the following Thursdays:

Venue: The Royal Society of Arts, John Adam Street, London, W.C.2., *except 7th December.*

Time: 7.30 p.m.

7th December 1967, *at Havelock Arms, Gray's Inn Road, London W.C.1.*
Lucent syrops tinct with cinnamon
Dr. V. L. S. Charley (Beecham Products U.K.)

4th January 1968
Synergism of antimicrobials
Dr. E. E. Boehm (Nipa Laboratories Ltd.)

1st February 1968
(Joint Meeting with British Society of Perfumers and Aerosol Group, Institute of Packaging)
Perfuming aerosol products

7th March 1968
The problems of Parliament
D. Smith (Beecham Group Ltd.)

2nd May 1968
Some rheological aspects of cosmetics
B. Warburton and B. W. Barry (School of Pharmacy, University of London)

MEDAL LECTURE: Friday, 22nd March 1968
Eye sweet in cosmetic colours
Dr. B. H. Crawford (Imperial College of Science and Technology, London, S.W.7.)

1968 DINNER AND DANCE: Friday, 9th February, at the Russell Hotel, Russell Square, London, W.C.2.

ANNUAL GENERAL MEETING: Monday, 20th May 1968, at the Washington Hotel, Curzon Street, London, W.1. at 7 p.m.

SYMPOSIUM ON TECHNICAL DEVELOPMENTS IN COSMETIC PACKAGING

A Symposium covering new developments in the Packaging field with particular reference to Cosmetics and Toiletries is planned for 25th to 27th March 1968, at Harrogate, Yorks.

Anyone interested in presenting a paper is asked to contact Mr. Gatland, c/o Gibbs Proprietaries Ltd., Joseph Watson & Sons Works, P.O. Box 167, Leeds, Yorks.

SYMPOSIUM ON MANUFACTURING AND PROCESSING

A Symposium on Manufacturing and Processing will be held at the Town Hall, Royal Leamington Spa, Warwicks., on 13th and 14th November 1967. Participation is permitted only when application has been made on the appropriate form, and the fee duly paid. This is £5.5.0 for each participant who is a member of one of the Societies of Cosmetic Chemists affiliated to the I.F.S.C.C. The registration fee for non-members is £8.8.0. Registration forms giving all details are available from the General Secretary,.56 Kingsway, London, W.C.2. **The closing date for registration is 16th October 1967.**

Monday, 13th November 1967

Afternoon

14.15 "Expansion and the manufacturing function in the cosmetic industry"
J. P. SLATER, B.Sc., F.R.I.C. (*Avon Cosmetics Ltd., Northampton*).

14.45 "Considerations influencing a contract filler when packing a customer's product"
T. E. JONES, B.Sc. (*Serta, Ltd., Barking, Essex*).

15.15 Tea

15.30 "Production quality and processing—Some unusual case histories"
R. CLARK, F.R.I.C. (*Unilever Ltd., London, E.C.4*).

16.00 "Mixing and dispersion techniques"
R. G. BAINES, A.M.I. MECH.E., and G. COPE, A.I. CERAM. (*Steele & Cowlishaw Ltd., Stoke-on-Trent*).

18.45-19.30 Civic Reception by the Mayor of Leamington Spa, Alderman M. KERRY, at the Town Hall (Informal Dress).

19.45 Symposium Dinner, at the Regent Hotel

Tuesday, 14th November 1967

Morning

09.00 "Some experiences in developing a votator plant and process"
C. PUGH, B.Sc., F.R.I.C.

09.30 "The practical application of some theoretical considerations to the technology of emulsions"
J. F. BURBRIDGE, A.R.I.C. (*Honeywill-Atlas Ltd., Carshalton, Surrey*)

10.00 "The role of perfume in the manufacture of cosmetics"
DR. R. FAVRE (*Firmenich S.A., Geneva, Switzerland*)

10.30 Coffee

10.45 "The changing pattern of aerosol filling"
W. RILEY (*Midland Aerosols Ltd., Wolverhampton*)

11.15 "The dispersion of pigments into dry powder base—A comparison between three mechanical methods"
T. A. BROCK, B.Sc., F.R.I.C. (*Yardley of London Ltd., Basildon, Essex*).

11.45 "Modern lipstick base manufacture"
P. D. W. DALEY, F.R.I.C. (*Gala Cosmetics Group Ltd., Surbiton, Surrey*)

12.15 Lunch at Regent Hotel

Afternoon

14.15 "Results of an experimental study of the use of amphoteric detergents for shampooing"
DR. G. LIETZ (*Henkel International GmbH., Düsseldorf, Germany*).

14.45 "Manufacturing toilet soap for the cosmetic industry"
D. C. TOWNSEND (*The Standard Soap Co. Ltd., Ashby-de-la-Zouch, Leics.*)

15.15 Tea

15.30 "An introductory note to tablet making practice and machine design"
K. W. HARGROVE (*Manesty Machines Ltd., Speke, Liverpool 24*).

16.00 "Seven years of problems and progress"
R. D. PURSER (*Northampton & County Association for the Blind, Northampton*).

Wednesday, 15th November 1967

Morning

Visit to Avon Cosmetics Ltd., Northampton.

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