PERMANENT WAVING OF HUMAN HAIR: THE COLD PROCESS*

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APPROXIMATELY one-half billion dollars will be spent during the current year by American women for permanent waves, yet the scientific literature contains only few and scattered references to chemical and physical studies of the process of permanent waving. To those who are familiar with the subject this is not at all surprising, for it should be realized that permanent waving as an industry is relatively young, and a robustly growing and expanding industry is not particularly well suited to provide the equanimity and objectivity which are so conducive to fundamental studies. Then, too, in those few laboratories where fundamental studies have been carried out for a number of years, the workers involved are fully aware that they are studying one of the most profound subjects in biological chemistry, the chemistry and physiochemistry of proteins. It is, therefore, not at all surprising that they have been quite guarded in publishing and discussing the results of their studies. Furthermore, before much progress can be made in any field of scientific endeavor, tools and quantitative methods for evaluating experimental results must be developed and standardized. In the case of the chemistry of hair waving, few methods have yet found their way into scientific literature, although it can be stated with some degree of confidence that in the near future several will be published.

The desire of the human race to alter the natural pattern of the scalp hair is a rather strange phenomenon, for we find that among Europeans and Americans among whom straight hair is the rule, there is a pronounced desire for curly hair, whereas among negroes and others among whom curly hair is prevalent, the desire for straight hair is just as pronounced. It is only since the turn of the century that it has been possible to impart a more or less permanent curl to normally straight hair. Looking back now, we cannot help but admire the courage and ingenuity of Charles Nessler, the pioneer of the process of perma-

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nent waving of human hair (1). Since his empirical approach to the problem about 1906 and especially within the last few years, rapid and sound technological progress has been made so that today the process of permanent waving may be termed both an art and a science.

The morphology of human hair fibers is adequately treated in textbooks of histology and will only be touched upon here. Figure 1 shows a diagrammatic sketch of a section of hair fiber, while Figs. 2 through 5 are photomicrographs of human hair fibers both normal and damaged. Since the average scalp may contain either a preponderance of resistant or of damaged hair, it will be appreciated that the chemist in formulating waving lotions must exercise a great deal of judgment.

Permanent waving may be broadly subdivided into two

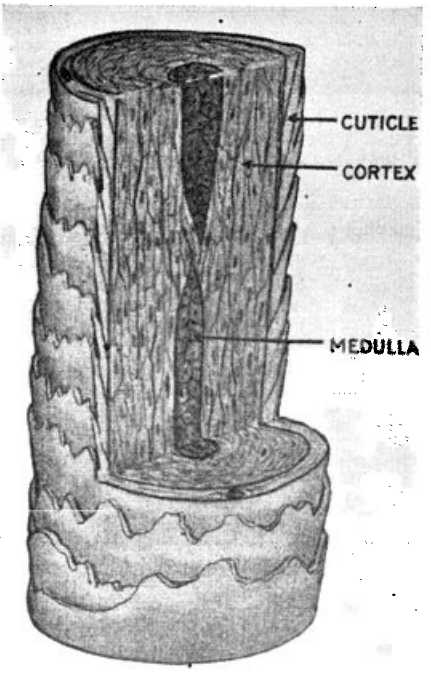

Figure 1.—Diagrammatic sketch of a section of a hair fiber. (From the *American Hairdresser Magazine*)

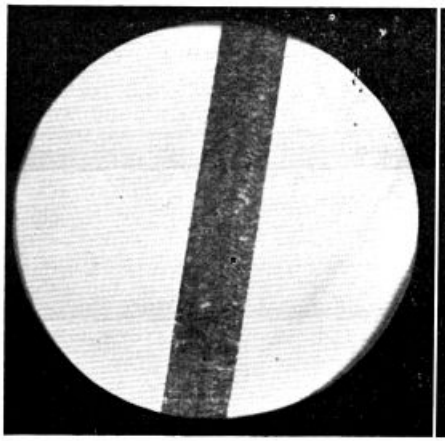

Figure 2.—Photomicrograph of normal hair fiber. 55 × magnification. Basic fuchsin stain

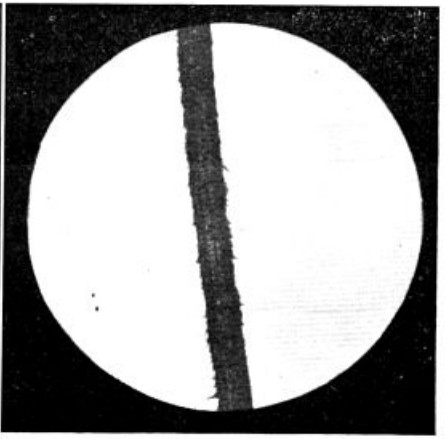

Figure 3.—Hair fiber showing physical damage to the cuticle. Fibers such as this will not "hold" a wave satisfactorily. 55 × magnification. Basic fuchsin stain

Figure 4.—Hair fibers showing trichorrhesis nodosa. Hair such as this will tend to show breakage during a waving process. 55 × magnification. Basic fuchsin stain

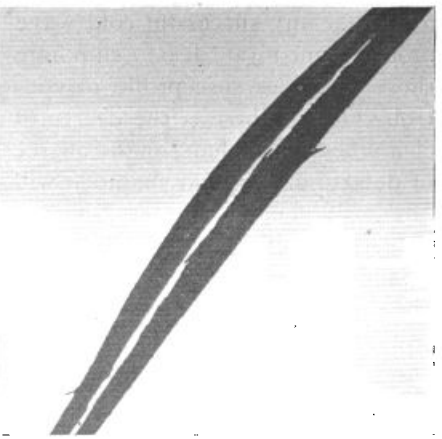

Figure 5.—Damaged fiber showing longitudinal splitting. 50 × magnification. Basic fuchsin stain

classes—hot and cold—both attaining the same end but differing in approach. In the hot method the hair is treated with an alkaline sulfite solution and wrapped around a rod of small diameter. Heat is then applied to transform permanently the hair from a straight to a curled state. Originally the heat was supplied by means of electrical heaters, but in recent years chemical heating compositions giving off an accurately gauged amount of heat have, to a considerable extent, replaced the rather elaborate and involved electrical heating devices.

In the cold process of permanent waving the hair is similarly wrapped around a rod of suitable diameter either prior to or after treatment with an alkaline reducing agent such as ammonium thioglycolate. Without applying external heat, the hair is transformed from its straight state into a desirable undulation. When this has been accomplished, as determined by inspection of test curls, the undulations are permanently fixed in position by the application of a suitable oxidizing agent. This is a brief outline of the process. It will be of interest to discuss each step in greater detail.

Prior to giving any permanent wave, but particularly prior to giving a successful cold wave, it is essential that the hair be effectively cleaned. To the uninformed, soap is soap, and all that can be expected from any shampoo is that it remove the superficial dirt from the hair. But the modern shampoo is much more than just soap, and plays an important role in permanent waving. Any permanent waving process is burdened by many uncontrollable variables common to human hair. It is obvious, there-

fore, that any successful cold wave process must at least eliminate those variables susceptible to control. One of these is the degree of cleanliness of the hair, or the degree of defatting. A good shampoo will obviously remove surface dirt and epidermal debris, and it will also remove to a greater or lesser degree the surface coating of oil or sebum from the hair. Figures 6 and 7 show hair fibers removed from a head before and after an efficient shampoo. But modern synthetic detergents go beyond this. Hair or keratin, after all, is not chemically inert; it contains many polar groups which can react with anions or cations. Thus, Neville and Harris (2) have demonstrated that when samples of wool are soaked in soap solution there is a greater adsorption of cations than there is of anions. Furthermore, Steinhardt, *et al.* (3) have amply demonstrated in their studies on the combination of wool protein with acid and base that this is not a simple physical adsorption, but rather that keratins react with anions and cations chemically. Similar conclusions were reached by Speakman and Elliott (4) in their studies on the combination of wool with acids and acid dyes. It is evident, therefore, that the action of detergents on hair goes far beyond that of surface cleansing, in that they may combine with and modify the polar groups of the keratin, and thus influence the subsequent action of the chemicals used in the actual waving step.

In the cold permanent waving process the hair is divided into approximately fifty rectangular sections and the hair from each of these

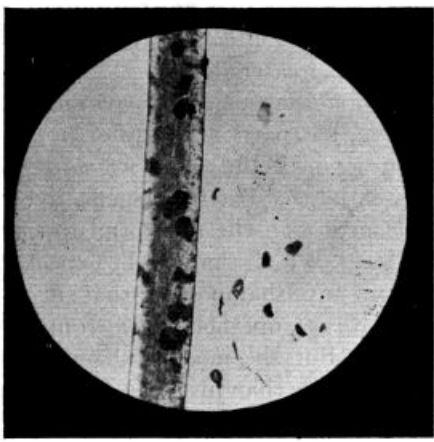

Figure 6.—Hair fiber taken before a shampoo, showing loose dandruff scales. 55 × magnification. Basic fuchsin stain

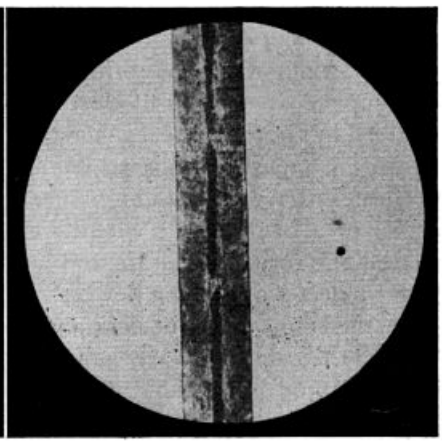

Figure 7.—Hair fiber taken after a shampoo from the same individual as that in Fig. 6. In this particular fiber the medulla is quite pronounced. 160 × magnification. Basic fuchsin stain

sections is wrapped around a plastic rod. The diameter of these rods may vary from 1/8 in. to 3/8 in. or more. A little reflection will prove that the diameter of the rod may influence the type of undulations produced in the permanent waving process, taking into consideration, of course, the fact that as the hair is wound around the rod the effective diameter will increase with each turn and the curvature will decrease. In terms of the strain introduced in the individual hair fibers, or rather the differential strain between the inner and outer periphery of each fiber, Table 1 lists some interesting calculations.

TABLE 1

Diameter (Inner Periphery Wrapped Fiber), In.	% Differential Extension Fiber Diameter 0.001 In.	0.005 In.
0.125	1.60	8.00
0.250	0.80	4.00
0.500	0.40	2.00

These data indicate that the per cent differential elongation is inversely proportional to the diameter of the curvature, either of rod or of rod plus hair if more than one turn of hair is placed around the rod, and directly proportional to the diameter of the hair fiber. (The above considerations show that the physical process of wrapping does or can influence the subsequent wave pattern.)

In the systems of cold waving as currently practiced, the waving lotion is applied to the hair before it is wrapped around the rod. The strength of preparations now in use commercially may vary from about 0.4 *N* to 0.9 *N* with respect to ammonium thioglycolate as determined iodimetrically. The pH of these solutions may vary from 9.0–9.5. Usually the alkalinity of the solution is brought about by the addition of ammonium hydroxide. In view of the fact that the system ammonium thioglycolate–ammonium hydroxide is a fairly efficient buffer, considerable variations in concentration of free ammonia will produce only small changes in the pH of the system. Hence, it would seem more desirable to express the alkalinity in these cases in terms of the normality of free ammonia rather than in terms of pH. Bases other than ammonia may be used, but at present ammonium hydroxide seems to be preferred in commercial waving lotions.

It is obvious that in order to produce a chemical reaction within the hair fiber we must introduce the chemical agent into the fiber. Speaking in practical terms, the degree of alteration or reduction of hair in the cold wave process depends upon the amount of thioglycolate which diffuses into the hair and upon the rate with which this is accomplished. The amount of thioglycolate which is available for diffusion into a hair fiber is a function of the capillary air space between the fibers wrapped around the rod during a waving process.

In Fig. 8 is shown a diagram of a cross section of a tress of fibers in close packed relationship. In the

particular case illustrated, hair fibers of uniform diameter are assumed to form a rectangle ($RSTU$) with one side equivalent to a total of two hair fiber diameters ($2D_H$). Due to close packing the second dimension is somewhat less than this amount, and it can be shown readily that it is equivalent to $\sqrt{3}$ (D_H). Therefore the area of the rectangle $RSTU$ equals

$$A = 2(D_H) \times \sqrt{3}\ (D_H)$$

Since the equivalent of four fibers is inscribed in this rectangle the cross-sectional area of these hair fibers is given by the expression:

$$A' = \pi(D_H)^2$$

The ratio of the area of the rectangle to the area of the fibers included within the rectangle is given by the following equation:

$$\frac{A}{A'} = \frac{2\sqrt{3}(D_H)^2}{\pi(D_H)^2} = \frac{2\sqrt{3}}{\pi} = 1.1 \qquad (1)$$

It can readily be visualized that a tress of hair is made up of n rectangles, each containing four fibers.

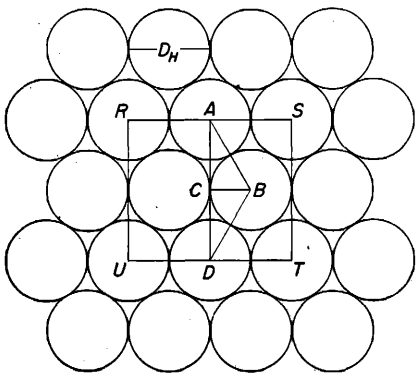

Figure 8

Introducing n in equation 1, it will be found that it appears both in the numerator and denominator and hence will cancel out. Equation 1 is therefore of general nature, applicable to any number of fibers. A consideration of the equation for the value of A' indicates that in a given cross-sectional area this value must remain constant regardless of fiber diameter. If this be true then it follows that the volume of air space must also remain constant. In any tress of hair therefore, the capacity of the curl for permanent waving lotion—if it is assumed that all air will be dispelled—is constant.

Assigning the term N to the total number of hair fibers in any cross section, the following relationship is arrived at:

$$N = \frac{A'}{\pi(D_H/2)^2} \qquad (2)$$

where A' equals the cross-sectional area of the hair fibers and D_H equals the diameter of each fiber.

A relationship between the reactive keratin surface (S) in terms of N, L (length of fibers) and D_H may then be established by the following equation:

$$S = \pi D_H \times L \times N \qquad (3)$$

Inasmuch as the value for N varies inversely with the square of the radius of the hair fibers, it will be seen that the reactive keratin surface in a tress will be profoundly affected by the fiber diameter. For example, if the hair diameter is doubled, the number of fibers in a given cross section will be reduced to one-fourth the previous numbers. Accordingly

the keratin surface would be reduced by 50%.

In deriving these equations it was assumed that all hair fibers are of uniform diameter and are wrapped in a uniform close packed arrangement. It need not be emphasized that these conditions are idealized and are seldomly realized under actual waving conditions.

In hair undergoing a cold wave treatment in which the tress is saturated with ammonium thioglycolate, the following reaction takes place:

$$\text{Hair—S—S—Hair} + 2\text{HSCH}_2\text{COONH}_4 \rightleftharpoons 2\ \text{Hair-SH} + \text{NH}_4\text{OOCCH}_2\text{—S—S—CH}_2\text{COONH}_4$$

In the above equation Hair—S—S—Hair is used to represent a normal segment of a keratin molecule as shown in Fig. 9.

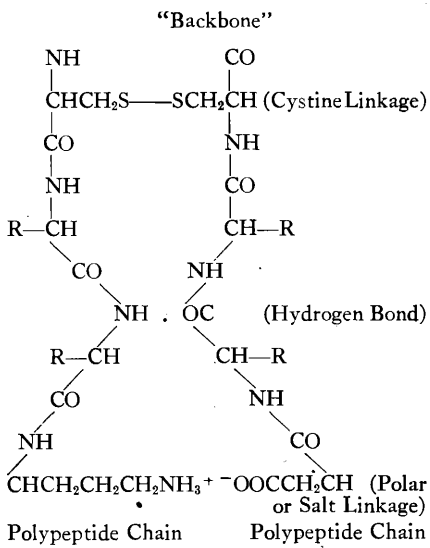

Figure 9

Hair—SH is used to indicate this segment after the reductive splitting of the disulfide bonds. Several methods have been used to follow the reduction of the disulfide bonds in hair undergoing a cold waving treatment. The Sullivan cystine method (5) as modified for this problem in this laboratory (6) has been very helpful in following the action of thioglycolates on hair. Table 2 shows the results obtained in one of these studies.

TABLE 2—EFFECT OF TIME ON THE DEGREE OF REDUCTION OF HUMAN HAIR USING A COMMERCIAL COLD WAVING SOLUTION (DCR-3) AT ROOM TEMPERATURE

Reduction Time, Min.	Cystine Found, %	Av.
0—Control	17.0	
0—Control	16.0	16.5
4	3.0	
4	2.9	3.0
8	2.6	
8	2.6	2.6
14	2.4	
14	2.6	2.5
20	2.5	
20	2.4	2.5

It should be pointed out that in these studies small tresses of hair (about 1 gm.) were reduced for the time stated by immersing them in a beaker containing a commercial cold wave lotion (—SH = 0.72 *N*; pH = 9.2, at room temperature). The results show that under these rather drastic conditions the reduction is practically complete within four minutes and further treatment has very little effect upon the residual disulfide linkages. It should not be concluded from this experiment, however, that the same degree of reduction is obtained during the process of cold waving, for in this particular experiment a huge excess of ammonium thioglycolate

was available, whereas under normal waving conditions the amount of thioglycolate is limited by the ratio of capillary air space to the amount of hair on the curling rod, as pointed out before. It should also be realized that this amount of reduction is not necessary or even desirable in actual practice. One-fourth the amount of reduction observed in Table 2 is probably the degree of reduction obtained in an average cold wave.

In Fig. 9 linkages other than the covalent disulfide bonds are indicated. These hydrogen bonds and salt linkages must play some role in the process of cold waving.

To them must be added the van der Waals' attractive forces which exist between the non-polar side chains. In studying the process of cold waving it becomes of importance to determine how much each of these forces contributes to the ability of a fiber to resist deformation. It has been pointed out by Sookne and Harris (7) in their study of wool fibers that van der Waals' forces vary inversely as the sixth or higher power, whereas Coulomb forces will vary inversely as the square of the distance. It is to be expected, therefore, that in the process of deforming a fiber several different forces will have to be overcome. In experiments carried out in this laboratory this subject was investigated. Single hair fibers were stretched in water, 0.1 *N* HCl, and 5 *N* monochloracetic acid, and the load-elongation curve plotted. Since it is known that water will not affect salt linkages or hydrogen bonds significantly, dilute HCl will affect salt linkages only, and 5 *N* monochloroacetic acid will rupture both salt linkages and hydrogen bonds (8, 4), the load-elongation curves of fibers thus treated reveal the magnitude of these individual forces in keratin.

Figures 10 and 11 show the results obtained when fibers were elongated under these conditions. It is quite evident from Fig. 10 that in the case of 0.1 *N* HCl the load required to stretch the fiber has been reduced, indicating the amount that the salt linkages contributed to the fiber strength. Much more pronounced is the effect of the hydrogen bonds, for when these are broken, as with 5 *N* monochloroacetic acid, the resistance of the fiber to deformation drops precipitately (Fig. 11). That no permanent change has been introduced in the fiber by the chloroacetic acid

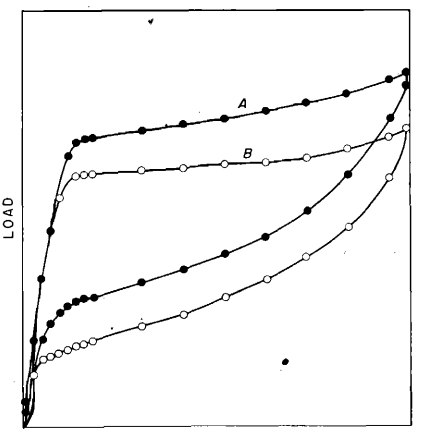

Figure 10.—Stress strain curve. 20% elongation in 0.1 *N* HCl. *A*—original water curve, *B*—in 0.1 *N* HCl

treatment is also shown in Fig. 11, curve *C*. This curve was obtained from the same fiber which gave

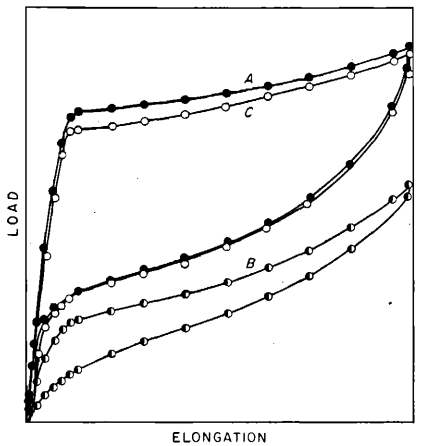

Figure 11.—Stress strain curve, 20% elongation in 50% monochloracetic acid (wt./vol.). *A*—original water curve, *B*—in monochloracetic acid, *C*—water curve 24 hours after *B*.

curve *B* after the chloroacetic acid had been washed out. As shown, the fiber has nearly regained its former state, indicating that the co-ordinate valences were reformed as soon as the chloroacetic acid was removed.

Bull and Gutmann (9) have advanced a very plausible theory to explain the shape of the load-elongation curve which is obtained when a human hair fiber is deformed. They visualize the hair protein in the form of a thixotropic gel which under the influence of a stress induced by elongation will be converted into a sol. This transformation is brought about by the severance of salt linkages and hydrogen bonds. The obvious implication is that if these bonds are ruptured by chemical means, less elongation is required to change the keratin to the sol state and thus induce plastic flow.

Hysteresis loops such as shown in Figs. 10 and 11 may seem far removed from practical cold wave problems. However, such is not the case, for it will be recalled that one of the steps in giving a cold wave consists of wrapping the hair around a rod, that is, inducing a strain in the hair fiber. It is immaterial that this happens to be differential strain in which one side of the fiber is stretched more than the other. From a practical standpoint it would seem important, therefore, to design a process which would co-ordinate the effect of the lotion as a whole on the secondary valence forces with the effect of the thioglycolate on the covalent disulfide bonds. It is of interest in this connection that Jones and Mechan, (10) studying the dispersion of keratins, stress the view that the splitting of the disulfide bonds and of the co-ordinate bonds in keratin are processes which can take place independently.

A direct result of the severance of bonds in the keratin molecule, be they primary valence bonds or co-ordinate bonds, is the swelling of the hair fiber. It is true that hair fibers will swell to a degree when placed in pure water, yet this is very small compared to the swelling which occurs when hair fibers are placed in a medium which is known to sever bonds, such as an alkaline thioglycolate solution or a concentrated solution of monochloracetic acid.

Since in swelling the cross-sectional diameter of the hair fiber increases, it is evident that individual polypeptide chains of the keratin molecules are separated by a distance greater than exists in dry fibers. This separation, the result of the rupture of the various bonds, will allow a greater degree of movement of the side chains, both polar and non-polar, permitting their uncoiling or reorientation with respect to the "backbone" or main peptide chains.

The final step in any process of cold waving consists of fixing the undulation produced by the wrapping of the hair around the curling rod and the subsequent action of the alkaline thioglycolate solution. Offhand, this would seem to be a very simple step since the oxidation of the sulfhydryl groups alone may produce the desired effect. In actual practice this reoxidation is produced by the so-called neutralizing or fixing lotions. Essentially these are dilute solutions of oxidizing agents such as potassium bromate, hydrogen peroxide, potassium iodate, etc. If the fundamental aspects of this step are examined carefully, it soon becomes evident that it is far from being simple, and in fact it is as involved as the other steps in cold waving. One purpose of this step is to reorient the amino acid side chains in positions comparable to those which they had had before the ammonium thioglycolate was applied. Then, too, the swelling of the hair fiber must be reversed, the sulfhydryl groups of the hair must not only be oxidized but reoxidized to disulfides, and salt linkages and hydrogen bonds must be reformed in such a manner that the hair will retain its curled state even when exposed to the action of repeated shampoos and the elements.

As was pointed out before, keratin which has been swelled and reduced by the action of ammonium thioglycolate shows a good deal more randomness in the arrangement of the amino acid side chains than untreated hair. When such hair is treated with an oxidizing agent such as bromate or peroxide, disulfide bonds will be reformed. The amount of rebuilding of these bonds will be a function of several variables, such as concentration of the oxidizing agent, time of contact, and temperature. In Table 3 the effectiveness of a commercial 3% potassium bromate solution in oxidizing reduced hair is shown. In this particular experiment a sample of hair was reduced with ammonium thioglycolate to a cystine content of 2.5–3.0%. The hair was then reoxidized by immersing it in a beaker of 3% $KBrO_3$ at room temperature for the time stated. It can be seen from this table that the reaction is nearly complete within a short time and further oxidation did not increase the amount of cystine significantly. It should be pointed out, however, that the method for evaluating the degree of reoxidation (6) determined only the amount of cystine existing at any time and does not tell if any

of this cystine had been oxidized further. In other experiments rebuilding of cystine linkages up to 100% of the original has been obtained, although the average amount of rebuilding (in many experiments in the beauty shop) is about 85%.

TABLE 3—EFFECT OF TIME ON THE DEGREE OF REOXIDATION OF REDUCED HUMAN HAIR

Oxidation Time, Min.	Cystine Found, %	Av.
0—Control not reduced	16.1	
0—Control not reduced	15.1	15.6
3	10.2	
3	10.3	10.3
6	11.9	
6	12.0	12.0
9	12.1	
9	12.4	12.3
15	13.2	
15	13.2	13.2

Considerable work has been done on the oxidation of sulfhydryl compounds and disulfides by various workers. Thus, Stoves (11) has contended that cystine links of keratin fibers are first hydrolyzed by aqueous solutions of oxidizing agents and the sulfur is then oxidized to sulfuric and sulfonic acid residues. Rutherford and Harris (12) working with wool, came to the conclusion that the action of hydrogen peroxide on keratin consists of the oxidation of the disulfides with the formation of disulfoxides and similar compounds. In another paper these authors (13) suggest that the disulfide sulfur of wool, exposed to the irradiation of a carbon arc, even in an atmosphere of nitrogen will be oxidized in part to sulfuric acids. Lemin and Vickerstaff (14) also agree with Harris and co-workers that the action of hydrogen peroxide on keratin leads to the oxidation of disulfide bonds. It seems, therefore that oxidation of hair or keratin does not necessarily stop at the cystine stage but will frequently go beyond it. This is a point well worth remembering when evaluating the efficacy of fixative or "neutralizing" agents.

Experimentally, it is possible to follow the oxidation of sulfhydryl groups in hair quantitatively much more easily than to follow the other changes which occur in hair as a result of the oxidation step. It has been pointed out before that one of the actions of ammonium thioglycolate is to swell the hair. In such hair it would seem that some of the pairs of sulfhydryl groups are separated too far to allow their reoxidation to disulfides. The work of Phillips and his coworkers (15) on the oxidation of thioglycolate reduced wool by oxygen also indicates that oxidation of sulfhydryl groups to disulfides may not be as smooth a process as is generally conceived.

It can be visualized that when reduced hair is treated with an excess of oxidizing agent, be it hydrogen peroxide, bromate, or iodate, some of the sulfhydryl groups will be in a fortuitous position so that they can be oxidized immediately to disulfides. Others will not be so situated and either will not be oxidized at all or will be oxidized to sulfuric or sulfonic residues. The number of disulfide bonds formed may be sufficient to give the hair a more or less permanent set. Yet due to insufficiency of —S—S— bonds formed

and the effect of the secondary valence bonds which eventually will be re-established in the fiber plus the tendency to a higher state of entropy, considerable strain is placed on the reformed disulfide bonds and it is therefore not surprising that in actual beauty shop practice the relaxation of a "permanent" wave is not uncommon.

Certain commercial waving processes have been designed to overcome this difficulty. In these processes an absorbent pad is placed around each curl after the waving lotion (ammonium thioglycolate) has acted sufficiently long and before the fixative (oxidizing) solution is applied. These pads withdraw the excess waving lotion from the spaces between the fibers by capillary action. By removing the excess thioglycolate from the outside of the fiber without removing significant amounts of solution from within the fiber, they tend to reverse the action of the reducing agent. A little reflection will readily show that at the end of the reducing step the ratio of dithiodiglycolate to thioglycolate is higher within the fiber than it is outside of the fiber. Going back to the equation showing the reaction of hair with thioglycolates given at the beginning of this paper, it can certainly be expected that the reaction will not go any further to the right, but since it is an equilibrium reaction and it so happens that the Redox potentials of cysteine/cystine and thioglycolic acid/dithioglycolic acid systems are the same (16), it may be reversed.

Under the influence of the adsorbent pads we thus may have a partial reoxidation, which under optimum conditions may be sufficient to give some permanent set to the hair. The contribution of the absorbent pad to the success of the cold wave is more than inducing the reoxidation of sulfhydryl group. By withdrawing the waving lotion from the air spaces surrounding the hair fibers and rebuilding some disulfide linkages, the adsorbent pads initiate the deswelling of the hair fibers. Since this is a gradual and controllable process, it allows the amino acid side chains to reorient themselves in positions which are more favorable to the formation of desirable salt linkages and hydrogen bonds. But beyond this, the slow deswelling action of the absorbent pads permits the sulfhydryl groups which were spacially too far separated to be oxidized to disulfides to be brought into juxtaposition so that they can be thus oxidized.

Briefly stated, the function of the absorbent pad is therefore the initiation of the rebuilding of the covalent —S—S— bonds, the gradual deswelling of the hair fibers thus allowing the establishing of desirable coordinate valence bonds, and the bringing together spacially —SH groups, which would otherwise be resistant to oxidation to disulfides.

In the discussion of the chemistry of the cold wave process the picture has been intentionally oversimplified. In the treatment of various steps it has been assumed that the hair fiber possesses a homogeneous

structure. This obviously is not true. As yet very little is known as to what role the cuticle, the cortex, and the medulla play in the process of cold waving. Until such time as more data and new experimental tools become available, it seems advisable to use the oversimplified concept to further the understanding of the cold wave process. The recent publications by Phillips (8), Stoves (11, 17), Lehmann (18), Mercer and Rees (19), Hock and McMurdie (20), and others indicate that the problem of the structure of keratin fibers as related to their chemical reactivity is receiving more and more attention.

Current widespread interest in the toxicological properties of thioglycolates has revealed the fact that very few experimental data on this subject have been published. It is obvious that neither eloquent editorials nor vociferous accusations or denials will lead to the solution of the problem.

In private correspondence from clinicians, several of these have stated that they have patients which show "typical" symptoms of thioglycolate poisoning. It is strange that these "typical" symptoms which one clinician describes, often differ radically from those described by another clinician. As yet no authoritative work has been published on the mode of action of thioglycolate on the living organism and on the symtomatology of thioglycolate poisoning. In this laboratory, using rabbits as test animals, it was found that it is possible to kill the animals if sufficiently large doses of ammonium thioglycolate are applied percutaneously over a long enough time. When the organs and tissues of animals which had thus succumbed were examined macroscopically and microscopically by a competent pathologist, no pronounced changes from the normal controls could be observed. Work now in progress suggests the attractive hypothesis that the action of thioglycolates may be to deprive the body of labile methyl groups (from methionine and choline), these being used to detoxify the thioglycolate. In this connection, it is interesting to note that thiodiglycolic acid, given either percutaneously or orally by stomach tube, seems to be quite well tolerated by experimental animals.

Percutaneous applications of moderate amounts of thioglycolates are readily tolerated by experimental animals. Using the Draize technique (21) it was found that the daily application of a commercial cold wave lotion for twenty days in amounts equivalent to 100 ml. per 50 kg. of body weight produced no apparent ill effects on rabbits as evidenced by the growth curve, red and white cell counts, as well as examination of the organs at necropsy. While it is not justifiable to translate these findings directly to the human being without further work, they do seem to indicate that the factor of safety is quite large, since only a very small fraction of 100 ml. can possibly be absorbed by the patron during a cold wave.

Patch test studies using the Schwartz and Peck method (22) have shown that the incidence of sensitization to cold waving lotion is quite small, and that when the concentration of thioglycolate is kept below 1 *N*, the danger of primary irritation is negligible. More than 400 patches were applied to employees, some of whom come in contact with thioglycolates daily, while others have come into contact with the material only occasionally, and still others had never been exposed to it before. Out of this relatively large series, only one definite positive (+) response has been obtained.

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