ACTION OF SOAP ON SKIN

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I. PATCH TESTS WITH FATTY ACIDS

In spite of rather extensive experimentation on the action of soap on the skin, the mechanism of this reaction is still undetermined. Is the fatty acid, the alkali or some added ingredient (perfume, dye, filler) the active etiologic agent of soap irritations? Does soap act as an allergen or as a primary irritant? Definite answers to these questions are still lacking.

Recently it has been shown that the skin has the power to neutralize externally applied alkali. Thus, the alkali in any soap residue on the skin is neutralized and the fatty acids of the soap remain on the skin at approximately the p_H of the cutaneous surface. It therefore seems important to determine the action of the fatty acids on the skin. Furthermore, the fatty acids come into contact with the skin at a higher p_H than that normal for the skin during continuous contact with soap, and the action of the fatty acids at an increased p_H then becomes important. This paper will present data on the action of fatty acids on the skin at normal and altered hydrogen ion concentrations. It is hoped that such data will help to explain the mechanism of the action of soap on the skin.

By definition, a soap is the salt of an alkali and a fatty acid. In the soaps most commonly used the alkali is either sodium or potassium hydroxide, both of which are strongly alkaline. The fatty acids vary with the type of oil used to produce the soap. Those most frequently present belong to three groups: (1) the saturated fatty acids, particularly caproic, caprylic, capric, lauric, myristic, palmitic and stearic (acids of even-numbered carbon atoms, increasing from 6 to 18 in the order given); (2) the unsaturated fatty acids, particularly oleic and linoleic, and (3) the hydroxy fatty acids, such as ricinoleic acid. All of these are weak acids. Since a soap is the salt of a strong alkali and a weak acid, a water solution of the soap hydrolyzes to produce an excess of hydroxyl

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ions and, therefore, an alkaline solution results, even though the soap contains chemically equivalent amounts of alkali and acid.

Almost all investigators of the problem of soap irritations have concerned themselves with the question of whether the alkali or the fatty acid is the offending agent. Stauffer [1] and also Jordan, Walker and Osborne [2] concluded that the alkali is not the important factor because patch tests gave no indication that the more alkaline soaps are the more irritating ones. But it must be remembered that in addition to the variation in alkalinity, different soaps also vary in the types of fatty acids they contain. The fact that in these tests the intensity of reaction to the patch test is not directly proportional to the alkalinity of the soap does not of itself indicate that the alkalinity of the soap is not a contributory factor. As a matter of fact, some of the data in the paper by Osborne and his co-workers might be interpreted to indicate that the alkalinity is an important factor. They made patch tests of solutions of two concentrations of the same soap, and frequently the more concentrated one gave the more intense reaction. Such patch tests might be considered to be patch tests with the same fatty acids at different concentrations of alkali, in which the higher concentration gave the more intense reaction.

Mayer [3] stated the opinion that the alkali is the causative agent in soap irritations. Gardiner [4] found cottonseed and coconut oil soaps more irritating than palm and tallow soaps, but instead of investigating the relative activity of the varying fatty acids of these soaps, he concluded that the two former require a higher equivalent of alkali to saponify, and when this is liberated from such soaps, it necessarily has a more injurious action on the skin.

Goldman [5] concluded from a series of patch tests that pure coconut oil soap is more irritating than other soaps but did not attempt to explain why it is more irritating. Hansen [6] found that patch tests with such

1. Stauffer, H.: Die Ekzemproben (Methodik und Ergebnisse), Arch. f. Dermat. u. Syph. **162**:517-576, 1931.

2. Jordan, J. W.; Walker, H. L., and Osborne, E. D.: Studies in the Eczematizing Properties of Soaps, New York State J. Med. **36**:791-795, 1936.

3. Mayer, R. L.: Toxicodermien, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1933, vol. 4, pt. 2; cited by Goldman, L.: The Skin Reactions of Infants and Children to Soaps, J. A. M. A. **108**:1317-1320 (April 17) 1937.

4. Gardiner, F.: Soaps and Their Effects on the Skin: An Analytical Research, Edinburgh M. J. **8**:514-520, 1912.

5. Goldman, L.: Patch Tests with Soaps, M. Bull. Univ. Cincinnati **7**:90-92, 1935.

6. Hansen, P.: Einige Untersuchungen über die Einwirkung der Seife auf der Haut, Acta dermat.-venereol. **17**:589-596, 1936.

substances as sodium oleate, "sapo medicatus" (in water and petrolatum), and "sapo kalinus," or soft soap (in water and petrolatum), showed frequent mild irritations on both normal and eczematous skin. The most irritating material was 50 per cent soft soap in petrolatum. Hansen expressed the belief that this irritation was caused by the excess alkalinity of this soap. He found 10 per cent solutions of sodium palmitate and sodium stearate nonirritating. In this work, as in the work of Jordan, Walker and Osborne,[2] emphasis was placed on the concentration of the patch test material.

Hansen, following the work of Burckhardt,[7] further showed that the skin has the power of neutralizing the alkali present in the soap. In the patch tests with weak solutions of soap, it is logical to assume, therefore, that shortly after application the alkali is neutralized by an acid stronger than the fatty acids present in the soap. It is also possible that when the patch test material is a strong solution of soap in water (gel), or solid pieces of soap, or soap in petrolatum, a "case-hardening" effect may occur in which the fatty acids are quickly precipitated in the layer of patch test material adjacent to the skin. Since, therefore, in a final analysis patch tests with soaps may be considered to be patch tests with fatty acids, the alkali of the soap having been neutralized relatively quickly by the skin, it seemed advisable to make a series of patch tests with the pure fatty acids in an attempt to explain better the mechanism of the action of soap on the skin.

Pusey[8] stated: "Another class of chemical irritants which frequently produce dermatoses are decomposing body secretions. The fatty acids and other products of decomposition are irritating and occasionally the causes of dermatitis." Hailey[9] reported an irritation caused by mimeograph oil, of which he expressed the opinion that the active ingredient was oleic acid. Cronin[10] reported irritations due to a mixture used in the manufacture of rubber, in which he expressed the belief that the irritating ingredient was stearic acid. One may well question in the last two instances whether sufficient tests were made to prove definitely that the fatty acids were the injurious substances. No other reference concerning the direct action of the fatty acids on the skin has been found.

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7. Burckhardt, W.: Beiträge zur Ekzemfrage: Die Rolle des Alkali in der Pathogenese des Ekzems speziell des Gewerbeekzems, Arch. f. Dermat. u. Syph. **173**:155-167, 1935.

8. Pusey, W. A.: The Principles and Practice of Dermatology, ed. 4, New York, D. Appleton and Company, 1930, p. 73.

9. Hailey, W. H.: Dermatitis from Oleic Acid, Arch. Dermat. & Syph. **8**: 530 (Oct.) 1923.

10. Cronin, H. J.: Lead Stearate Poisoning in the Rubber Industry, Boston M. & S. J. **192**:900, 1925.

We have performed patch tests on about 200 persons with normal and pathologic skin with single fatty acids [11] and with mixtures of fatty acids. Since these fatty acids are almost insoluble in water, they were used only in the pure form. The patch tests were applied to the upper part of the arm, where there were no apparent lesions, and allowed to remain in contact with the skin for about twenty-four hours. They were read about one hour after the patches were removed. The results of these tests are shown in the accompanying table.

The mixed fatty acids from coconut oil were chosen because coconut oil is frequently used for the manufacture of soap and because it represents primarily a mixture of saturated fatty acids. It contains a much higher percentage of the fatty acids of low molecular weight than most fats used in soap making. The mixed fatty acids from

Percentage of Positive Reactions to Patch Tests with Fatty Acids

	Normal Subjects			Soap-Irritable Persons			Patients with Contact or Atopic Dermatitis		
Fatty Acid	Number	Positive	%	Number	Positive	%	Number	Positive	%
Caproic	99	63	68.7	24	17	70.9	63	50	79.4
Caprylic	99	96	97.0	25	24	96.0	65	64	98.5
Capric	99	84	84.9	25	23	92.0	64	53	82.8
Lauric	103	9	8.7	26	14	53.8	108	35	32.4
Myristic	103	3	2.9	26	4	15.4	106	11	10.4
Palmitic	100	3	3.0	26	6	22.1	99	9	9.1
Stearic	102	6	5.9	26	6	22.1	107	12	11.2
Mixed (cocoanut oil)	102	85	83.3	26	26	100.0	106	82	77.3
Oleic	92	2	2.2	16	1	6.3	96	12	12.5
Mixed (castor oil)	90	0	0	16	0	0	87	6	6.9

castor oil were chosen because of the high percentage of hydroxy fatty acid present. Some work was done with the mixed fatty acids from linseed oil, primarily unsaturated fatty acids, but the results are not reported here, because it is felt that the rapid oxidation of these acids makes the results unreliable.

The three groups of persons tested represent: (1) those who were free from any disease of the skin and had no history of soap irritation; (2) those who had normal skin at the time of the test but had had pruritus or vesiculation after the use of some soap or soaps, and (3) a group of persons who had cutaneous lesions characteristic of either contact or atopic dermatitis at the time of the test. The first two groups were made up principally of female nurses between the ages of 19 and 26 years. The third group was heterogeneous as to age and occupation but consisted principally of persons in whom some external con-

11. All were Eastman organic chemicals except the oleic acid.

tact was thought to be one cause of the dermatitis. The group included a large number of persons with characteristic "housewife's dermatitis" on the dorsa of the hands.

No attempt has been made to separate the positive reactions into groups according to their intensity. A majority of the reactions consisted of erythema only. More intense reactions (papules or vesicles) were sometimes seen from caproic, caprylic, capric and lauric acids and from the mixed fatty acids of coconut oil. The patients frequently complained of itching while these five materials were in contact with the skin. Caproic and caprylic acids frequently produced pigmentation which did not disappear for several weeks.

It is at once apparent that the saturated fatty acids of low molecular weight (caproic, caprylic and capric) are more irritating than the acids of higher molecular weight. It is likely also that the presence of these acids in the mixed fatty acids of coconut oil accounts for the almost universal irritation caused by patch tests with this material. No explanation for the slightly lower percentage of positive reactions to caproic than to caprylic acid is apparent at present.

Positive reactions to lauric, myristic, palmitic, stearic and oleic acids are less frequent. In the case of these acids there is an apparent small increase in the percentage of positive reactions obtained among persons with dermatitis as compared with normal persons, and the reactions of these persons are usually more intense than those of persons with normal skin. The apparent high percentage of positive reactions to lauric, palmitic and stearic acids among the "soap irritable" group is probably an error due to the small number of persons tested.

Oleic acid gives about the same percentage of positive patch tests as did the saturated acids of higher molecular weight. There is almost a complete absence of positive reactions to the mixed fatty acids from castor oil.

COMMENT

The results of patch tests with the fatty acids must not be directly compared with those of patch tests with soaps, reported by other investigators. The higher percentage of positive results obtained with saturated fatty acids of low molecular weight, as compared to the fatty acids of high molecular weight, lends support, however, to the belief that soaps made from oils containing these acids are more irritating than soaps made from oils containing acids of high molecular weight.

The high percentage of positive reactions to patch tests with the saturated fatty acids of low molecular weight does not necessarily indicate that these fatty acids are responsible for irritations due to the soap. Normal skins are also irritated by these acids; therefore, they

should be considered "primary irritants." The fact that the skin of most persons is not irritated by soaps probably indicates that there is only a small amount of these fatty acids in soaps.

Do the results of the patch tests with the fatty acids of a molecular weight higher than that of capric acid indicate that they are responsible for soap irritations? There is a sharp decline in the percentage of positive reactions to patch tests on normal skin for the acids having a molecular weight above that of capric acid. The percentage of positive reactions to these acids is not much greater, however, for persons with either contact or atopic dermatitis than for the persons with normal skin. It is believed that too small a percentage of the 100 persons with irritated skin showed positive reactions to patch tests with these acids to permit the conclusion that they alone are responsible for soap irritations. Strong reactions to these acids may be of diagnostic significance.

In all the tests reported in this paper, there has been no control of the p_H of the substances during the patch tests. In the next section of this paper the results of patch tests with fatty acids at controlled hydrogen ion concentrations will be reported. It will be shown that such tests more clearly indicate the parts played by the fatty acids and the alkali in producing soap irritations.

SUMMARY TO SECTION I

The results of patch tests on persons with normal and pathologic skin with the various pure fatty acids and mixtures of fatty acids indicate that:

1. Saturated fatty acids of low molecular weight yield a much higher percentage of positive reactions to patch tests than do acids of higher molecular weight.

2. Persons with normal skin give positive reactions to the fatty acids of low molecular weight as frequently as do persons with pathologic skin.

3. Fatty acids of a molecular weight higher than that of capric acid produce reactions somewhat less frequently on normal than on pathologic skin. Strong positive reactions to these acids may be of some diagnostic significance.

4. Positive reactions to the unsaturated fatty acid, oleic acid, occur about as frequently as do positive reactions to the saturated acids of high molecular weight.

5. A positive reaction to the mixed fatty acids from castor oil is seldom seen.

II. PATCH TESTS WITH FATTY ACIDS AT VARIOUS HYDROGEN ION CONCENTRATIONS

It was pointed out in the first part of this paper that even though a soap may be made from chemically equivalent amounts of an alkali and a fatty acid, an aqueous solution of that soap will have a p_H greater than 7 because the alkali of the soap is more strongly ionized than the acid. Actually, aqueous solutions of the commercial soaps tested show a p_H between 10 and 11 when measured with the glass electrode.

The cutaneous surface has been shown to have a p_H between 4 and 7.[12] When the skin is washed with soap and water and well rinsed, the resulting p_H of the surface is usually between 6 and 7.5. From this point, the p_H of the surface will slowly drop to normal if no more soap touches it. The rate at which the p_H of the surface returns to normal probably varies from person to person. Burckhardt [7] has attempted to measure the variation in the rate at which the skin will neutralize externally applied alkali. Using a modification of Burckhardt's technic, Hansen [6] observed the change in color of an indicator in a small quantity of soap solution held on the skin under cellophane. He found that phenolsulfonphthalein (phenol red) added to a 1 per cent solution changed color in five minutes, i. e., the p_H of the solution dropped to 6.5; a 10 per cent solution showed a change in color in seven hours.

A patch test with a soap solution should be considered to be a patch test with the fatty acids contained in the soap at a p_H which is continuously diminishing from about 10.5 to about 4.5. The time required for the p_H to become constant will depend on the concentration of the test material and the characteristics of the skin of the person tested. One questions, therefore, what part hydrogen ion concentration plays in determining whether the reaction to a patch test will be positive or negative. In order to determine this point, a series of patch tests has been made with single fatty acids at different hydrogen ion concentrations, each concentration being held relatively constant.

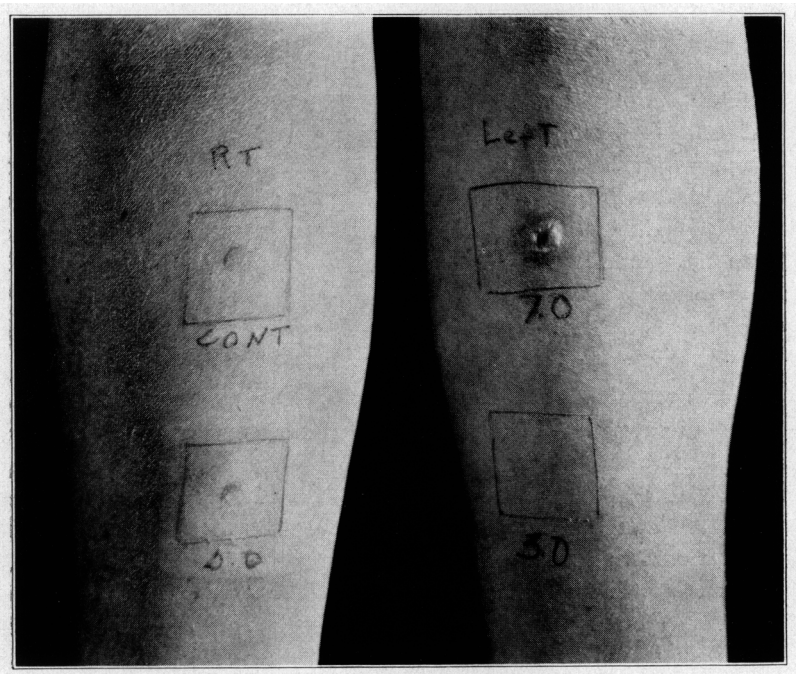
For this investigation a technic [13] was used whereby the fatty acid [14] was held in contact with the skin under a small piece of glass, secured with adhesive tape on three sides. The patient was given dropping bottles containing buffer solutions and was instructed to place a drop or so of the solution under the free edge of the glass every hour while awake. The patches remained in contact with the skin for twenty-four hours.

12. Blank, I. H.: Measurement of the p_H of the Skin Surface, J. Invest. Dermat., to be published.

13. Guild, B. T.: Window Patch Test, Arch. Dermat. & Syph., this issue, p. 807.

14. Eastman organic chemicals were used.

The fatty acids used for these tests have melting points higher than the cutaneous temperature but are easily melted at the temperature of boiling water. Therefore, a drop of the liquid fatty acid was placed in the center of the piece of glass, where it quickly crystallized and adhered firmly to the glass. Two types of standard buffer solutions have been used—that of Clark and Lubs [15] and that of McIlvaine.[16] Usually four tests with a single fatty acid were made on each patient—one "control" test, in which no buffer solution was added and three in which buffer solutions of p_H 3, 5 and 7, respectively, were added.



Reactions to the patch test with lauric acid at various hydrogen ion concentrations.

A p_H of 5 is approximately equivalent to the average p_H of the cutaneous surface. It is felt that with frequent contact with soap, a p_H of at least 7 may be maintained for some time. Also, a buffer solution having a p_H of 3 was used to determine whether in some of the

15. Clark, W. M., and Lubs, H. A., cited by Clark, W. M.: The Determination of Hydrogen Ions, ed. 3, Baltimore, Williams & Wilkins Company, 1928, p. 200.

16. McIlvaine, T. C., cited by Clark, W. M.: The Determination of Hydrogen Ions, ed. 3, Baltimore, Williams & Wilkins Company, 1928, p. 214.

cases, in which irritation was seen at the normal p_H of the skin, there would be diminished irritation at a lower p_H. The results of one such series of patch tests with lauric acid on the flexor surfaces of the forearms are shown in the accompanying photograph.

It is plainly evident from the photograph that the reaction to lauric acid at a p_H of 5 is approximately the same as the reaction when no buffer is added (control); when the p_H is increased to 7, the reaction is much more intense; when the p_H is reduced to 3 no reaction is apparent. A person was chosen to be photographed in whom this difference in reaction at various hydrogen ion concentrations was striking. Not all persons showed such a decided variation. However, in 56 of 64 persons, some of whom had no dermatitis, the reaction at 7 was definitely more intense than that at 5; and in 25 of 44 the reaction at 3 was definitely less intense than that at 5. In the majority of cases lauric acid was used, but both capric and myristic acids also showed this variation. Completely negative reactions have been obtained to palmitic acid at hydrogen ion concentrations of 5 and 8 in each of the 7 cases in which the substance was used.

One questions, of course, whether patch tests with the buffer solutions alone might not show these variations in intensity of reaction. In this connection, a case cited by Stauffer [1] in 1931 is of interest. After performing patch tests in a single case of "eczema" with phosphate buffer solutions of p_H 6.5, 7.35 and 8, he stated:

> Remarkable in this case are the patch tests with the solutions of varying p_H, in which the solution with the high p_H (8) gives the strongest reaction; 7.35, however, reacts less strongly and 6.5 only slightly. This action at different hydrogen ion concentrations, and, indeed, the fact that the reaction to the alkaline fluid is strong and the one to the acid fluid scarcely appears, has never to my knowledge been observed until now.

Stauffer's patches were left on for three days. By the technic used in my work, however, the tests are for twenty-four hours only. Stauffer found completely negative reactions to both 6.5 and 7.35 p_H buffer solutions at the end of one and one-half days. Frequent tests with my buffer solutions alone have never shown a positive reaction.

COMMENT

In using the patch test to determine the etiologic agent of contact dermatitis, one should attempt to duplicate as nearly as possible the actual conditions under which contact with the material takes place. Such was the rationale of Goldman,[17] who swabbed the skin of infants

17. Goldman, L.: The Skin Reactions of Infants and Children to Soaps, J. A. M. A. **108**:1317-1320 (April 17) 1937.

daily with 10 per cent soap solutions instead of using a single application of soap as a patch test. In view of the work of Burckhardt [7] and Hansen,[6] it is doubtful, however, that daily swabbings simulate the more or less continuous contact with soap solutions experienced by laundresses and dish washers, because, as these investigators showed, the skin quickly neutralizes the alkali in a single application of soap. It is difficult to state just what p_H is maintained during frequent contacts with soap. It is not improbable, however, that at least as high a p_H is maintained as is maintained by the patch test technic described, by which a buffer solution of p_H 7 was added at hourly intervals.

The results of patch tests with such a technic lead to the formulation of an interesting theory. In the first section of this paper it was reported that saturated fatty acids of low molecular weight are irritating to most skins. As the molecular weight increases above that of capric acid, the fatty acids, of themselves, become less irritating. If, however, the surface of an area of skin in contact with some of the nonirritating fatty acids is maintained at a p_H higher than normal, the skin becomes irritated. The method used for maintaining increased p_H has been shown not to irritate the skin. Since most of the soaps commonly used at present contain only small amounts of the fatty acids which are of themselves irritating, it is probable that soap irritations result from neither the fatty acids alone nor the alkali of the soap but from a combination of the two. Whether the fatty acid and the alkali act individually on the skin or whether they first combine to form one irritating compound is yet to be established.

Positive reactions to patch tests with the fatty acids at a p_H higher than the normal p_H of the cutaneous surface are not always of diagnostic significance. Many persons with normal skin will show positive reactions to patch tests with some of the fatty acids under these conditions. It is believed, however, that a negative reaction to the patch test by a person who has dermatitis indicates that soap is not an important factor in producing the dermatitis.

It is also believed not only that the irritating quality of the fatty acids decreases with increasing molecular weight but that the amount of alkali which must be added before a fatty acid becomes an irritant increases with the increasing molecular weight of the acid. That is to say, irritations can be produced by fatty acids of high molecular weight only if the p_H of the cutaneous surface is maintained either at a higher point or at the same point for a longer period than is required to produce irritations when acids of lower molecular weight are used. Data are now being obtained to test this theory. Such experiments, it is hoped, also will indicate a test which will accurately grade the degree of irritability of the individual skin to soap.

SUMMARY TO SECTION II

It has been shown by a modified patch test technic that certain fatty acids give a more intense reaction when maintained at a p_H of 7 than at a p_H of 5. Also, many instances of diminished reactions at a p_H of 3 have been observed. The theory is proposed that neither the alkali nor the fatty acid alone is responsible for the irritation produced by soap, but that each is a contributing factor, and that the higher the molecular weight of the fatty acid, the more alkali will be required before irritation results.

III. SULFONATED OILS AS SUBSTITUTES FOR SOAP

At present the question of whether soap of itself can be a sensitizing agent has not been definitely settled. Hansen [6] and Bonnevie,[18] after studying over 900 cases, stated that true hypersensitivity to soap does not exist. The few patients in their series who seemed to be hypersensitive to some commercial soap proved to be hypersensitive to the perfume, dye, antiseptic or filler in the soap and not to the soap itself. Sulzberger and Goodman [19] concurred in this opinion.

Even though hypersensitivity to soap may be rare, the use of soap in many cases of contact dermatitis is considered inadvisable, because it is felt that even if the soap is not the specific etiologic agent, it nevertheless prolongs an irritation after the direct cause is eliminated. Also, the patient with atopic dermatitis is frequently advised not to use soap. After finding that 41 per cent of his patients with "eczema" gave positive reactions to various soaps, Stauffer [1] stated: "On this basis, I now forbid almost all of my patients with eczema to use soap." In place of soap, the dermatologist usually recommends liquid petrolatum or a vegetable oil. These seldom irritate, but they are unsatisfactory detergents for long-continued use, and the patient is usually psychologically opposed to them. Recently, sodium hexametaphosphate has been proposed as a substitute for soap.[20] Also, Jones and Murry [21] have recommended petrolatum to which 2 per cent cholesterol has been added.

As has been shown in the previous sections of this paper, the results of various patch tests indicate that certain of the fatty acids contained in soap are, of themselves, irritating to normal skin and that others of the fatty acids become irritants when in contact with skin at a p_H higher than

18. Bonnevie, P., in discussion on Hansen.[6]

19. Sulzberger, M. B., and Goodman, J.: Allergy in Dermatology: A Critical Review of Recent Contributions, J. Allergy **9**:398-423, 1938.

20. Jones, K. K.; Murray, D. E., and Ivy, A. C.: Sodium Hexametaphosphate: Its Use for Certain Occupational Dermatoses, Indust. Med. **6**:459-462, 1937.

21. Jones, K. K., and Murray, D. E.: Effects of Cholesterol in Petrolatum on Loss of Water by the Skin and on Cleansing, Arch. Dermat. & Syph. **36**:119-130 (July) 1937.

that of normal skin ("alkalinized" skin). Since even a "neutral" soap tends to increase the p_H of the cutaneous surface, a soap to be nonirritating, according to this theory, must contain no fatty acids which will be irritating to the "alkalinized" skin and certainly no fatty acid which is of itself an irritant to the skin at a normal p_H. Such a soap, according to my data from patch tests, would be a soap made from palmitic and stearic acids only. Hansen's [6] data also indicate that sodium palmitate and sodium stearate are nonirritating.

Clinical tests with soaps containing only very small amounts of any acid of a lower molecular weight than palmitic acid have been disappointing. Certain minor irritations of the skin, such as mild erythema or slight desquamation (dryness), have responded well to the substitution of special soaps made from palmitic, stearic and oleic acid for commercial soaps. (Practically all commercial soaps contain some coconut oil soap in which are some of the acids of low molecular weight.) Many of the more severe irritations, however, have not been benefited.

A detergent which would not "alkalinize" the skin and which contains no fatty acid which would irritate the normal "unalkalanized" skin would, therefore, seem to be desirable. Some of the more recently developed sulfonated alcohols and sulfonated oils appear to be such detergents. Biederman [22] and Goldman [5] have reported positive reactions to patch tests with a salt of a sulfonated alcohol. Schwartz [23] and Osborne and Putnam [24] have reported irritations due to "sulfonated oils" used in the textile industry. In neither instance, however, was the type of sulfonated oil determined.

The term "sulfonated oil" does not indicate a single compound but is frequently used to name any compound or group of compounds arising from the action of sulfuric acid on an oil or fat which is partly unsaturated. Thus, olive oil, castor oil, teaseed oil, cod oil, tallow, liquid petrolatum and many other oils can be sulfonated. Also, they may be sulfonated to different degrees, and the sulfonation procedure may be such as to produce many different side reactions. Consequently, it is difficult to evaluate reports of irritation due to "sulfonated oils." It is important, furthermore, not to confuse sulfonated oils with oils or ointments to which sulfur has been mechanically added. During the process of sulfonation the hydrophilic sulfate group is introduced into the oil molecule, which makes the oil "water soluble." Sulfur in the form of

22. Biederman, J. B.: Sensitivity to Drene Shampoo, New England J. Med. **217**:1088-1089, 1937.

23. Schwartz, L.: Actual Cause of Dermatitis Attributed to Sox, Pub. Health Rep. **49**:1176-1185, 1934.

24. Osborne, E. D., and Putnam, E. D.: Industrial Dermatoses, with Special Reference to Allergy and Mycotic Dermatitis, J. A. M. A. **99**:972-977 (Sept. 17) 1932.

the sulfate group has none of the properties of free sulfur. Thus, the sulfonated oils to be considered here are acidic "water-soluble" detergents and should not be confused with the sulfur medicaments now in common use.

Anhydrous sulfonated olive oil, produced so as to be practically free from side reactions, showed mild positive reactions to patch tests of 13 of 100 persons (13 per cent) with normal skin, of 3 of 26 persons (11.5 per cent) with a history of soap irritation but no lesion at the time of testing, and of 14 of 102 persons (13.7 per cent) with contact or atopic dermatitis. This sulfonated olive oil was chosen, therefore, as a soap substitute for clinical trials in cases of contact or atopic dermatitis. A few preliminary trials indicated that a mixture of this sulfonated olive oil and water, though satisfactory as a cleanser, "dried" the skin too much.

Instead of the sulfonated oil and water, a mixture of approximately 25 per cent sulfonated mixed olive and teaseed oils, 25 per cent liquid petrolatum and 50 per cent water was used.[25] This mixture also is produced so as to be practically free from those ingredients which result from side reactions during sulfonation. Dyes and perfumes are intentionally omitted. This material has the following specifications:

Specific gravity	0.98 to 1 at 25 C. (77 F.)
Refractive index	1.40 to 1.42 at 25 C. (77 F.)
Cold test	2 C. to 5 C. (35.6 F. to 41 F.)
Iodine value	9 to 10
Saponification value	45 to 55
SO_3 content	3 to 3.5 per cent
p_H (2 per cent aqueous solution)	6 to 7

The majority of subjects chosen for use of this detergent had contact dermatoses, although some had atopic dermatoses. Among the patients with contact dermatitis there were many housewives with lesions primarily on the dorsa of the hands. These patients were asked to use the oil mixture as a detergent, exclusive of any soap if possible. This was not possible in all cases. The patient was advised to rub the oil mixture on the areas to be cleaned and then to rinse it off with water. The material does not lather, but it cleans well. This detergent has been used in approximately 150 cases for periods varying from a few weeks to two years. Almost all the patients were ambulatory, and the extent to which directions were followed could not always be determined. Seldom was this substitution the only treatment given. Even with 25 per cent liquid petrolatum present in this specific mixture, some patients complained of excessive "dryness," though almost all of them thought that the skin was much less dry than when soap was used. In less than

25. This product ("acidoleate") was supplied by the National Oil Products Company, Harrison, N. J.

10 per cent did relapses occur coincidentally with the use of this sulfonated oil mixture, and in not all of these could it be proved that the use of the oil caused the relapse. In 18 of the 150 cases, after an improvement with the use of the oil, relapses were produced by asking the patient to return to the use of soaps. The irritation again cleared with the omission of soap and return to the use of oil.

At present it has not been shown that this oil mixture has any specific therapeutic value. It does seem, however, to be a detergent with which the patient can maintain satisfactory personal hygiene and which has been nonirritating in over 90 per cent of the cases. The patient may object to the lack of lather, but he much prefers this sulfonated oil mixture, which he can wash off, to a mineral or vegetable oil insoluble in water.

SUMMARY TO SECTION III

In 150 cases of contact or atopic dermatitis a mixture of 25 per cent sulfonated mixed olive and teaseed oils, 25 per cent liquid petrolatum and 50 per cent water, which has a p_H of approximately 6.5, has been substituted for soap. Most of the patients have found this sulfonated oil mixture a satisfactory detergent. Irritations have followed the use of the material in less than 10 per cent of cases. In 18 cases in which there were remissions with the use of the oil mixtures, relapses occurred when soap was again used. The oil mixture is not thought to have specific therapeutic value but rather to act as a means of maintaining satisfactory personal hygiene without soap.

Dr. B. Thurber Guild, of the allergy department, and the staff of the dermatologic department of the Massachusetts General Hospital assisted in these investigations.