A STUDY OF THE ALLERGENIC CONSTITUENTS OF LANOLIN (WOOL FAT)*

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Lanolin (wool fat, adeps lanae, wool wax, degras) is defined in the United States Pharmacopeia XIII (1947) as: "the purified anhydrous, fat-like substance from the wool of sheep."

This fat-like substance is in many respects analogous to human sebum in its biologic function and chemical composition. It occurs as an external coating on wool, is removable by commercial processes and has many uses. Practically all civilized men, women and children encounter lanolin almost daily. Although extensive analytical work has been done on the constitution of the wool fats and a voluminous literature exists on the subject, all their individual constituents have not yet been identified. It is, however, established that lanolin is a complex mixture, composed chiefly of fatty acid esters of high molecular weight alcohols (1, 2, 3, 4, 5, 6).

REASONS FOR UNDERTAKING THE PRESENT INVESTIGATION

Allergic eczematous contact-type sensitivity to lanolin occurs surprisingly rarely when one takes into account the multitudinous exposures of millions of persons to this substance. For lanolin is used not only in a great many dermatologic medicaments but also in innumerable non-medical materials—for instance, in cosmetics, hair tonics, soaps, shoe polishes—to name but a few.

Nevertheless, when hypersensitivity to lanolin does occur, it presents great problems to both physician and patient, precisely because of the manifold guises and disguises in which this material is constantly encountered. It might, therefore, be of great practical value to discover precisely the constituent or constituents which are the sensitizing allergens of lanolin.

But the identification of the allergens of lanolin may well have far more fundamental significance. If, for example, it were shown that some constituent common to both lanolin and to human sebum was the offending allergen in patients with allergic eczematous dermatitis to wool fat, this would represent another example of human hypersensitivity to body-own or autogenous materials.

The senior author has long been interested in the possibility of derivatives of the skin epithelia or the secretions of the skin glands acting as skin sensitizing antigens, and in turn, producing reactions in the skin itself. (See, for example, Ref. 7.)

Thus, the studies here reported were undertaken not only for practical reasons but also to ascertain whether lanolin-sensitive persons were allergic to a fat-like

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or lipoidal compound normally found in the human body or in or on the human skin. Such a finding might suggest new avenues for investigating the pathogenesis of numerous important diseases, including cancer and arteriosclerosis as well as many persistent dermatoses of unknown cause.

TEST MATERIALS EMPLOYED

As stated above, lanolin is a complex mixture. We are indebted to Dr. H. Ehrhardt and Mr. John Koczwara of the Botany Mills, Inc., for furnishing us with one of the samples of lanolin together with the lanolin constituents or fractions which they have isolated from it. In addition to this group of substances from the Botany Mills, the following were also employed in our tests:

1) lanolin from two other sources

2) cholesterol derived from the spinal cord of cattle

3) a common proprietary ointment-base, which is described as "a mixture of liquid and solid aliphatic hydrocarbons and alcohols obtained by the saponification of wool fat."

4) the carbon tetrachloride which was used as a solvent for the patch test materials.

These materials were employed for patch testing in the concentrations listed below. The tests were applied in orthodox fashion and removed, read and recorded approximately 48 hours later.

	Concentration
1) lanolin fatty acids (Botany)	1 % solution in carbon tetrachloride
2) mixed lanolin alcohols (Botany)	1 % solution in carbon tetrachloride
3) pure lanosterol (Botany)	1 % solution in carbon tetrachloride
4) lanolin fatty acids plus mixed lanolin alcohols (½% of each)	1 % solution in carbon tetrachloride
5) carbon tetrachloride	as is
6) a popular proprietary ointment base presumably including lanolin alcohols	as is
7) lanolin A (supplied by Botany)	as is
8) lanolin B (supplied freshly by a New York Pharmacy)	as is
9) lanolin C (which had been in a jar on our routine 'therapeutic patch test tray' for several weeks)	as is
10) cholesterol B (Botany—derived from lanolin)	1 % solution in carbon tetrachloride
11) lanosterol (Botany)	1 % solution in carbon tetrachloride
12) cholesterol A (derived from the spinal cord of cattle)	1 % solution in carbon tetrachloride

The cholesterol derived from the spinal cord of beef cattle was employed as a control for the lanolin-derived cholesterol which might conceivably have been contaminated by traces of other allergenic material from the sheep.

The 'pure lanosterol,' a more refined product than the plain lanosterol, was received just before the testing period started so that it as well as the lanosterol was used.

The 'mixed lanolin alcohols' is that mixture of alcohols which is present in lanolin before lanosterol (a tetracyclic-terpene derivative) and cholesterol have been removed.

A mixture of lanolin fatty acids and mixed lanolin alcohols was also used because we could not be sure, *a priori*, that such a *combination* was not necessary for eliciting the allergic response.

Finally, a commonly used proprietary base containing lanolin derivatives was included as a test substance in order to ascertain what, if any, allergenic relationship existed between such bases and lanolin.

TABLE I

	CONTROLS			TEST SUBJECTS (having eczematous allergic reactions to lanolin)			
	I	II	III	Mrs. R. T.	Miss L. C.	Mr. M. R.	Mr. H. G.
1. Lanolin fatty acids	0	0	0	0	0	0	0
2. Mixed lanolin alcohols	0	0	0	++-+++	+-++	++	+-++
3. Pure lanosterol	0	0	0	0	0	0	0
4. Lanolin fatty acids plus mixed lanolin alcohols	0	0	0	++	++	++	+-++
5. Carbon tetrachloride	0	0	0	0	0	0	0
6. Proprietary base	0	0	0	++-+++	++	++-+++	+-++
7. Lanolin A	0	0	0	+	+++	++	+
8. Lanolin B	0	0	0	+	+++	++	+-++
9. Lanolin C	0	0	0	++-+++	+++	++	+-++
10. Cholesterol B	0	0	0	0	0	0	0
11. Lanosterol	0	0	0	0	0	0	0
12. Cholesterol A	0	0	0	0	0	0	0

0 = no reaction
\+ = erythema
++ = erythema and edema
+++ = erythema, edema and vesiculation.

SUBJECTS STUDIED AND RESULTS OF TESTS

In order to rule out primary irritancy, three persons chosen at random were tested with the materials applied to the normal skin as patch tests in the above specified concentrations. In no instance did any of the substances cause any skin reaction whatsoever. Thereupon, four persons, who had been previously proved to react with an allergic eczematous contact-type dermatitis after a forty-eight hour contact with *lanolin*, were patch tested with the twelve substances selected for this investigation. In each instance, a distinctly positive reaction was elicited by each of the lanolin preparations, by the proprietary ointment containing lanolin alcohols, by the mixed lanolin alcohol fraction and by the lanolin fatty acid-mixed lanolin alcohol fraction. None of the other materials tested caused any skin reactions. These results are recorded in detail in Table I and illustrated in Figure I.

CLINICAL DATA ABOUT TEST SUBJECTS

Mrs. R. T., when seen during her first visit, presented an allergic eczematous contact-type dermatitis on the skin around the lips as well as a cheilitis exfoliativa. Patch testing with suspected materials led to the discovery that a lipstick,

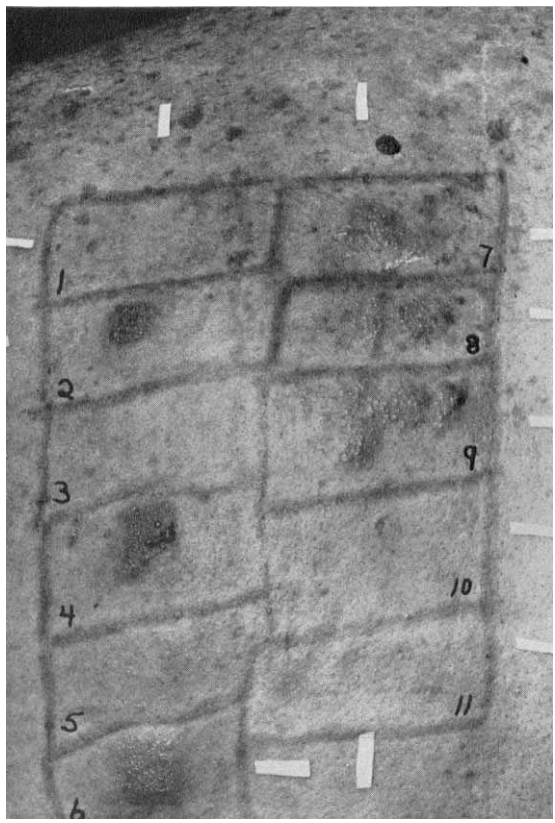

FIG. 1. Patch test reactions to eleven test substances on back of Mr. M. R. Each of the patch test areas has been enclosed within a rectangular outline.

Left Side		*Right Side*	
1. 0	Lanolin fatty acids	7. ++	Lanolin A
2. ++	Mixed lanolin alcohols	8. ++	Lanolin B
3. 0	Pure lanosterol	9. ++	Lanolin C
4. ++	Lanolin alcohols plus lanolin fatty acids	10. 0	Cholesterol B (derived from lanolin)
5. 0	Carbon tetrachloride	11. 0	Lanosterol
6. ++ to +++	Proprietary base (presumably including lanolin alcohols)		

(Photo taken about 48 hours after application of the tests and about 2 hours after their removal and reading)

and on further analysis, the lanolin component of the lipstick, was the offending allergen.

Miss L. C. and Mr. M. R. were under treatment and were suspected of having an allergic eczematous contact-type of hypersensitivity to lanolin when careful

observations and histories revealed that an eczematous reaction followed the use of each lanolin-containing medicament. These suspicions were confirmed when each responded with a strong eczematous reaction to patch tests with lanolin.

Mr. H. G. was reported by Sulzberger and Morse (8) as having an allergic eczematous contact-type of skin reaction to lanolin in 1931. Now, nineteen years later, this man still reacts positively on contact with lanolin applied in the standard patch test method. Over the past nineteen years, his chronic lichenified eczema of the hands has persisted and it is interesting that this man's occupation is one which entails the daily handling of woolens. (In many types of woolen cloth, a very small percentage of wool fat is left on the fibers in order to permit them to retain their resiliency; perhaps the constant contact with this small amount of lanolin has sufficed to cause patient H. G.'s dermatosis to persist all these years).

SUMMARY AND INFERENCES

1. Four persons proved to have an allergic eczematous contact-type hypersensitivity to lanolin, were patch tested with lanolin itself and with the compounds which represent the major groups of substances known to constitute wool fat.

2. Each of the subjects reacted to three different samples of lanolin and also gave eczematous contact-type responses to the mixed alcohol fraction and to all mixtures containing this alcohol fraction. No reactions were elicited by any of the other fractions of lanolin used for testing in this study.

3. The results show that in these four unselected lanolin-allergic subjects the immunologically active agent (the responsible allergen) was a constituent or constituents of the *mixed alcohols of wool fat;* and was not present in the other fractions such as the mixed fatty acids, cholesterols or the lanosterols.

4. Each subject reacted positively to contact with a common and widely-used proprietary ointment base, indicating that it probably contains the mixed lanolin alcohol fraction as its allergenic component.

5. One subject tested to lanolin by the standard patch method in 1931 and again in 1950, reacted on each occasion with an allergic eczematous contact-type of response. It is likely that this man has retained his allergic eczematous contact-type hypersensitivity to lanolin throughout the nineteen years; although one cannot rule out the possibility of his having lost and then regained this hypersensitivity one or several times in the interval between the testings.

6. Since we could not ascertain the exact chemical nature of the culpable ingredient in the mixed lanolin alcohols, nor discover whether the allergenic agent was present also in human skin or sebum, our present studies failed to shed further light on the important problem of possible skin sensitization to autogenous products of human epithelia, sebum or other normal products of the human body.

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