

Lanolin Allergy: History, Epidemiology, Responsible Allergens, and Management

Bailey Lee and Erin Warshaw

Allergy to lanolin has been recognized by dermatologists for decades. This review summarizes the history, epidemiology, and allergenicity of lanolin and its derivatives. "The lanolin paradox" and the safety of pharmaceutical-grade lanolin products are also discussed.

DURING THE LAST SEVERAL DECADES, allergic contact dermatitis from lanolin and its derivatives has been debated. Questions regarding the prevalence, the precise antigen(s), and the detection of lanolin allergy have all been posed.^{1,2} In spite of a global research effort, many of these questions remain unanswered. The goal of this review is to summarize the existing literature on allergic contact dermatitis from lanolin. Differing viewpoints on the epidemiology, allergenic components, proper detection, and sources of exposure to lanolin from historical, present, and future perspectives are discussed.

Description and Composition of Lanolin

Lanolin is a substance derived from secretions of the sebaceous glands of sheep and functions as a protective coating on wool. This fatlike substance, also called wool grease, may constitute 5 to 25% of the weight of sheared wool. Wool grease is modified to create lanolin and its derivatives. In 1986, Barnett described the chemical structure of lanolin as a wax made of a "highly complex mixture of esters, di-esters, and hydroxyl esters of high molecular weight lanolin alcohols and high molecular weight lanolin acids."³ Lanolin alcohols can be broken down further into three main chemical groups: aliphatic alcohols, sterols (including cholesterol), and trimethyl sterols. Lanolin acids are made up of four groups: normal, iso, anteiso, and hydroxyl acids. A mixture of free alcohols constitutes roughly 12% lanolin in addition to trace amounts of free acids and hydrocarbons⁴ (Table 1).⁵

From the University of Minnesota, Minneapolis, MN, and the Veterans Affairs Medical Center, Minneapolis, MN.

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Although advanced techniques have been used to determine the nature of many of these components, a large portion of the esters in lanolin have yet to be characterized.

A major difficulty in fully characterizing lanolin is that its composition varies. Breeds of sheep, geographic locations, methods of extraction, and levels of purification may differ. These potentially important variations have several implications in regard to the components of lanolin that cause sensitization in humans. Another problem in understanding allergy to lanolin is that many previous studies have not fully described the lanolin type, allergens, and concentrations or the clinical relevance of positive reactions. For the purpose of this review, we have included details if provided by the authors of the original study. Information not reported is identified as such in the text.

Brief History of Lanolin

The ancient Greeks were likely the first to extract crude wool fat from the wool of sheep. Documentation from 700 BC describes a process of boiling wool in water with extraction of the top layer of grease. A more refined method was discovered in 60 AD by the Greek physician Dioscorides and consisted of pouring wool washings into a receptacle several times until a froth developed. After the froth disappeared, a layer of wool wax was collected.³ Dioscorides called this product "oesypus," and it became widely cited in several ancient medical texts and pharmacopeias.⁴

It was not until Otto Braun, a German, patented a method for centrifuging the scouring liquid derived from wool washings in 1882, however, that the term "lanolin," from the Latin words for wool (lana) and oil (oleum), was coined. Soon after this discovery, the large-scale production of lanolin began in Germany. This process then spread

Table 1. Composition of Raw Wool Wax and Pharmaceutical-Grade Lanolin

<i>Constituent</i>	<i>Raw Wool Wax (% weight)</i>	<i>Pharmaceutical Lanolin (% weight)</i>
Wax esters	75–90	97
Free alcohols	6–12	2.5
Free fatty acids	1–8	0.3
Water	1–5	0.05
Insoluble particulates	0.1–2	Negligible
Lipid-soluble salts	0.2–2	Negligible
Water-soluble salts	0.1–0.2	Negligible
Detergent residues	0.1–1	0.02
Pesticide residues	20–150*	0.8*
Polycyclic aromatic hydrocarbons	0.1–0.5*	Negligible
Peroxide value	N/A	12 [‡]
Color	Variable	Pale to dark yellow
Odor	Variable	Odorless

Adapted from Hoppe U.⁵*Values are in milligrams per kilogram⁻¹.[‡] = milliequivalents per kilogram⁻¹; N/A = not applicable.

to the United Kingdom, and by the end of the nineteenth century, wool wax was produced in most European countries.⁴

Modern methods for extracting lanolin from wool washings involve more sophisticated techniques, which can be grouped into three main categories: (1) modified centrifugation, (2) solvent extraction, and (3) “acid-cracking” (this involves adding acid to crude wax, which

destabilizes and separates the wax for easier filtering).^{5,6} Today, the most widely used method of wool wax extraction is the centrifugation process.⁵ The crude wool grease extracted by these processes is then purified and modified in numerous different ways to produce the plethora of lanolin products and derivatives.

Nomenclature

When discussing allergy to lanolin, it is important to understand the various terminology and synonyms that can be used. The different names and derivatives of lanolin are daunting; this review focuses on compounds commonly used in patch-testing clinics to detect lanolin allergy. Lanolin, in a general sense, refers to “adepts lanae,” the term used for purified wool fat as described above. It is also synonymous with “anhydrous lanolin” and the “wool fat” of the British Pharmacopoeia (BP) (Table 2). The “lanolin” of the United States Pharmacopeia is simply the addition of varying amounts of water to anhydrous lanolin. Eucerin (not the commercial cream marketed under the same name) is composed of paraffins and a mixture of sterols and alcohols obtained from wool fat. A more modern term for this product is “wool alcohols ointment BP.”^{4,5} The consumer product Eucerin (Beiersdorf, Hamburg, Germany) contains lanolin alcohols, petrolatum, mineral oil, water, and preservatives. This product is not to be confused with Eucerit (Beiersdorf), which is a purified lanolin alcohol product containing high concentrations of cholesterol. Amerchol L-101 (Amerchol, Edison, NJ) is often used in patch

Table 2. Constituents of Lanolin Products and Their Synonyms

<i>Product Name</i>	<i>Constituents</i>	<i>Synonyms</i>
Lanolin	Mixture of esters of alcohol and acids	Adepts lanae, anhydrous lanolin, wool fat BP
Lanolin USP	Anhydrous lanolin + water	Hydrous lanolin
Eucerin	Paraffins + sterols + wool fat alcohols	Wool alcohols ointment BP
Eucerin (Beiersdorf, Hamburg, Germany)	lanolin alcohols + petrolatum + mineral oil + water + preservatives	NA
Eucerit (Beiersdorf)	Purified Eucerin + cholesterol	NA
Amerchol L-101 (Amerchol, Edison, NJ)	lanolin alcohols + mineral oil, cholesterol, and sterols	Concentrated absorption base
Ameralk (Amerchol)	Alcoholic fraction of Amerchol L-101	NA
Golden Fleece	Purified anhydrous lanolin	NA
Decubal (Alpharma, Bridgewater, NY)	6% Golden Fleece + dimethicone + glycerol + isopropyl myristate	NA
Medilan (Croda, Yorkshire, UK)	Purified anhydrous lanolin (< 3% free alcohols and < 1 mg/kg pesticides)	NA

BP = British Pharmacopoeia; USP = United States Pharmacopeia; NA = not applicable.

testing today (Amerchol L-101 is now sold as Vilvanolin L-101 [Wickliffe, OH]). It is a concentrated absorption base composed of lanolin alcohols and mineral oil.⁷

Sources of Exposure to Lanolin and Its Derivatives

Touted for its emollient properties, lanolin can be found in a variety of toiletries, including lipsticks, cosmetic creams and powders, shaving creams, shampoos, and soaps. Ointment bases for topical medicaments are another common source of lanolin exposure.¹ Because of its ability to penetrate the epidermis to the depth of the stratum granulosum^{8,9} and into keratinocytes,⁵ lanolin has been prescribed for the treatment of many skin conditions, including xerosis, eczema, and open wounds.^{10–12} In addition, it has long been recommended as the treatment of choice for nipple soreness in lactating women.^{13–15}

Lanolin is also used for industrial purposes. Wool wax has been applied to metallic surfaces to prevent corrosion, added to ink to prevent crystallization, used in adhesive plasters, incorporated into furniture polish and shoe creams, and even applied to leather to enhance pliability and water resistance.¹ These sources represent potential allergenic exposures although a comprehensive literature search found only two case reports of lanolin dermatitis due to industrial products, one from metal coatings and the other from adhesive plaster.^{16,17}

Sheep wool and wool clothing are also important sources of exposure to wool wax, as the content of wool wax in clothing may be as high as that in some cosmetics.¹⁸ Despite this, reports of lanolin allergy among those working directly with sheep or in wool manufacturing are rare. Lord reported four cases of allergic reaction to wool: one with chronic urticaria, one with acute urticaria, and two with eczema. All were caused by contact with wool garments, and all had resolution of symptoms when wool contact was eliminated (patch testing was not performed).¹⁹ Another case of allergic contact dermatitis due to wool clothing was reported in Africa 2 years later.²⁰

History and Epidemiology of Lanolin Allergy

In 1922, a report described a German patient who developed a “skin reaction” to a cream that contained 6% wool alcohols.²¹ Seven years later, Ramirez and Eller documented the first patch-test-positive case of allergic contact dermatitis from lanolin.²² A handful of case reports of lanolin allergy were published during the 1930s,^{23–25} but it was not until the 1950s, when several studies verifying the prevalence of lanolin sensitivity in

dermatologic patients were published, that lanolin allergy became widely recognized. (Key studies are summarized in Tables 3 to 5.) Sulzberger and colleagues documented lanolin allergy in 1.14% of 1,048 patients with suspected contact dermatitis in 1953 whereas Baer and colleagues reported a higher rate (4.4%) in 637 dermatologic patients who used hydrous wool fat in 1955.^{26,27} In 1961 and 1962, Hjorth and Trolle-Lassen reported that 1.8% of 1,878 patients had positive patch-test reactions to Eucerin (not further defined) and that 1.6% of 1,664 patients reacted to wool alcohols (30% in petrolatum [pet]).²⁸ Bandmann and colleagues reported a prevalence of 3% in 1972, similar to Mortenson’s findings in a separate study in 1979.^{29,30}

In 1982, the North American Contact Dermatitis Group (NACDG) published a 13-year study on reactions to cosmetics. Of 8,093 patients who were patch-tested for suspected contact dermatitis, 487 (6%) were designated as having contact dermatitis from cosmetics. Results of tests with lanolin, lanolin alcohol, or lanolin oil were positive in 20 (4.1%) of the 487 patients who were determined to have contact dermatitis from cosmetics.³¹ Another study showed that 66 of 616 patients with dermatitis were found to be sensitive to wool alcohols and/or Amerchol L-101 (AL-101).³² More recently, a retrospective study of patch-test patients in the United Kingdom showed a higher positivity rate of 4.9%.^{33,34} Wakelin and colleagues found the prevalence to be lower in a large population of Londoners. They reviewed the patch-test results of 24,449 patients tested with 30% wool alcohols and quoted a positivity rate of 1.7%.³⁵ In the NACDG summary for 2003 to 2004, 113 (2.2%) of 5,145 patients undergoing patch testing for suspected contact dermatitis reacted to lanolin alcohol 30% pet. Current relevance (definite, probable, or possible) was 28.6%. This percentage of lanolin-positive patients was unchanged from that reported for 2001 to 2002 and was not significantly different from values reported for 1998 to 2000 (2.4%), 1996 to 1998 (3.3%), or 1994 to 1996 (3.3%).³⁶

To our knowledge, only one study has estimated the incidence (rather than the prevalence) of lanolin allergy in a general population (see Table 5). In 1975, Clark collected data from three European hospitals, estimated the patient population served by the hospitals, and then determined the number of new cases of lanolin alcohol sensitivity per year. The centers and the number of patients served in each were as follows: (1) Wycombe General Hospital (Buckinghamshire, UK), 225,000; Sahlgrenska Hospital (Gothenburg, Sweden), 350,000; and the University of Lund Department of Dermatology (Malmö, Sweden), 250,000. Within this aggregated population, 54.4 new

Table 3. Reported Prevalence of Positive Patch-Test Reactions to Lanolin and Its Derivatives in Dermatologic Patient Populations

<i>Author, Year, Country</i>	<i>Study Population</i>	<i>No. of Patients Tested</i>	<i>Antigen(s) Tested (Concentration)</i>	<i>% Positive</i>	<i>Relevant Positive Reactions (%)</i>
Sulzberger et al., 1953, USA ²⁶	Patients with various dermatologic conditions	1,048	Lanolin USP (as is)	1.14	NR
Baer et al., 1955, USA ²⁷	Dermatitis patients	637	Hydrous lanolin (as is)	4.4	NR
Hjorth and Trolle-Lassen, 1963, Denmark ²⁸	Eczema patients	1,664	Lanolin (as is)	0.6	NR
			Lanolin (as is, in 5% salicylic acid)	1.6	
			Wool alcohols (30% pet and olive oil)	1.6	
		1,878	Eucerin	1.8	
Wereide, 1965, Norway ⁶⁶	Eczema patients	270	Lanolin USP (in 5% salicylic acid) and/or Eucerin (in 5% salicylic acid)	7.4	NR
Epstein, 1972, USA ⁶⁸	Patients with suspected contact dermatitis	298	Wool wax alcohol (30% pet)	1.7	NR
Bandmann et al., 1972, Denmark, Germany, Great Britain, Sweden ²⁹	Patients with suspected dermatitis	4,000	Wool alcohol (30% pet)	3.0	NR
Mortenson, 1979, Denmark ³⁰	Eczema patients	1,230	Wool alcohols (30% in soft yellow paraffin)	2.7	NR
		899	Wool alcohols (30% in soft yellow paraffin)	3.2	
	Patients with various dermatologic conditions		Hydrogenated lanolin (30% in soft yellow paraffin)	0.2	
			AL-101 (as is)	3.5	
			Lanolin and/or its derivatives	6.6	
NACDG, 1982, USA ³¹	Cosmetic-related contact dermatitis patients	487	Lanolin*	2.2	NR
			Lanolin alcohol*	1.4	
			Lanolin oil*	0.4	
Henderson et al., 1995, UK ³³	Eczema patients	60	Wool alcohols (30% pet)	6.6	NR
			AL-101 (50% pet)	1.6	
			Eucerin (as is)	0	
Wakelin et al., 2001, UK ³⁵	Patch-test patients	24,449	Wool alcohols (30% pet)	0.9–2.3	38
		2,227	AL-101 (as is or 50%)	5.9	
			Eucerin (as is)	0.3–1.1	
	Facial dermatitis patients	7,367	Hydrogenated lanolin (as is)	0.5–2.0	
NACDG, 2003–2004, USA ³⁶	Patch-test patients	1,977	Lanolin alcohols (30% pet)	1.6	30.1

AL-101 = Amerchol L-101; NACDG = North American Contact Dermatitis Group; NR= not reported; pet = in petrolatum; USP = United States Pharmacopeia.

*Concentration not specified.

cases of lanolin alcohol sensitivity were detected per year. Applying certain exaggeration factors to account for the use of lanolin alcohols in place of lanolin, the use of

keratolytics with patch tests, and secondary versus primary lanolin sensitivity, Clark determined the annual incidence of lanolin allergy in the general population to be 1.46 to

Table 4. Reported Prevalence of Positive Patch-Tests Reactions to Lanolin and Its Derivatives in High-Risk Populations

<i>Author, Year, Country</i>	<i>Study Population</i>	<i>No. of Patients Tested</i>	<i>Antigens Tested (Concentration)</i>	<i>% Positive</i>	<i>Relevant Positive Reactions (%)</i>
Cronin et al., 1970, Denmark, Sweden, Germany, England ³⁷	Atopic patients Stasis dermatitis patients	233 302	Wool alcohols (30% pet) Wool alcohols (30% pet)	1.0 (11 men, 20 women)	NR
Wilson et al., 1997, UK ³⁸	Leg ulcer patients	81	Wool alcohols* AL-101* Eucerin*	23.4 14.8 6.2	NR
Gallenkemper et al., 1998, Germany ⁴⁰	Chronic venous stasis patients	36	Wool wax alcohols (30% pet) AL-101 (50% pet)	33.3 19.4	NR
Wakelin et al., 2001, UK ³⁵	Lower-leg dermatitis patients	918	Wool alcohols (30% pet)	6.0	NR
Machet et al., 2004, France ³⁹	Leg ulcer patients Patch-test patients without leg ulcers	106 36 256	Lanolin* Lanolin* Lanolin*	20.8 30.6 5.1	NR

AL-101 = Amerchol L-101; pet = in petrolatum; NR = not reported.

*Concentration not specified.

Table 5. Incidence and Prevalence of Positive Patch-Test Reactions to Lanolin and Its Derivatives in General Populations

<i>Author, Year, Country</i>	<i>Study Population</i>	<i>No. of Patients Tested</i>	<i>Antigens Tested (Concentration)</i>	<i>Positive Reactions</i>	<i>Relevant Positive Reactions (%)</i>
Sulzberger et al., 1953, USA ²⁶	Healthy volunteers	120	Lanolin USP	0%	NR
Clark, 1975, Great Britain ¹⁸	General population served by hospitals in Gothenburg, Lund, and Wycombe	825,000	Lanolin alcohol*	1.46–8.75 cases per million	NR
Kligman, 1983, USA ²	Healthy female volunteers	943	Hydrous lanolin USP (as is) Eucerin Wool wax alcohols (30% pet)	0% 0% 0%	NR

NR = not reported; pet = in petrolatum; USP = United States Pharmacopeia.

*Concentration not specified.

8.75 cases per million.¹⁸ Importantly, the relevance of these positive reactions was not discussed, and true incidence would best be determined by following known patch-test-negative patients over time.

Risk Groups

Patients with chronic dermatitis, especially lower-extremity venous stasis dermatitis, have been identified as a

high-risk population for the development of contact dermatitis from lanolin (see Table 4). A study evaluating contact dermatitis in atopic patients reported that in 80 men and 153 women, 1% of both groups had positive reactions to 30% wool alcohols. In contrast, the same study looked at 302 subjects (number by gender not reported) with stasis dermatitis and reported that 11% of men and 20% of women reacted to wool alcohols 30% pet.³⁷ Wilson and colleagues tested 81 patients with active

leg eczema with a number of different common sensitizers and found that wool alcohols (concentration not reported) were the most common allergens. Of the 81 patients, 24 (29.6%) reacted to lanolin, 19 reacted to wool alcohols, 12 reacted to AL-101, 5 reacted to Eucerin, and 12 reacted to some combination of the aforementioned products.³⁸ Other authors have reported rates that are more conservative; these include a 6.0% rate found in the aforementioned large retrospective study by Wakelin and colleagues.³⁵ Machet and colleagues looked at a smaller group of 106 patients with leg ulcers in Europe and found that 21% were sensitive to lanolin.³⁹ Gallenkemper and colleagues evaluated 36 patients with chronic venous insufficiency and found that 33% were sensitive to wool alcohols (30% pet) whereas 19% had positive reactions to AL-101 (see Table 3).⁴⁰

Relevance and Reproducibility of Positive Patch-Test Reactions to Lanolin

Several dermatologists have shown disdain for the idea that lanolin is a major sensitizer. Kligman stated in a 1998 article, "The hue and cry over the high frequency of lanolin allergy is an egregious example of misplaced zeal and science."⁴¹ This was a follow-up to his 1983 paper, in which he pointed out the lack of information regarding lanolin allergy in the general population, stating that sensitization rates in patients existed only for those with dermatitis. He quoted a study by Sulzberger and colleagues, who assessed 12 healthy subjects and found no positive patch-test reactions to anhydrous lanolin (as is).²⁶ In an attempt to address this issue, Kligman recruited 943 women with no history of skin problems to undergo patch testing with hydrous lanolin, Eucerin, and 30% wool alcohols in petrolatum. Excluding irritant reactions, none of the women had positive patch-test results. Kligman concluded that lanolin was a weak sensitizer and proposed that previously reported high prevalence rates were due to false-positive results, either from poor interpretation of patch tests or from hyperreactive skin (angry-back syndrome).²

Several studies have evaluated the reproducibility of positive reactions to lanolin. Edman and Moller found that only 20 of 33 patients with documented positive patch-test reactions to lanolin had positive reactions upon repeat testing.⁴² This loss of sensitivity to lanolin was also documented by Carmichael and colleagues, who reported that of 37 patients with prior positive patch-test reactions to lanolin, only 41% retained their sensitivity when retested 5 years later.⁴³ In a large multicenter German

study measuring concordance, 1,285 patients were patch-tested concomitantly on both sides of the back with 10 allergens, including wool alcohol 30% pet. Sixty-four (0.05%) had an allergic, questionable, or irritant reaction to wool alcohols (30% pet) on one or both sites of the back. Less than 30% of these 64 subjects had patch test results that read as allergic on both sites of the back whereas the largest percentage of subjects (38%) had an allergic reaction on one site and a negative reaction on the other.⁴⁴ Reasons proposed for the loss of patch-test positivity included false-positive primary test results, poor patch-test reproducibility, and loss of allergic contact response.⁴² Importantly, nonreproducibility or nonconcordance or both have been described with several antigens other than lanolin.⁴⁵⁻⁴⁷ Gollhausen and colleagues found that up to 44% of reactions to 39 antigens (including lanolin) in 35 patients were nonreproducible.⁴⁵ Brasch and colleagues double-tested 1,285 patients with 10 allergens, including lanolin, and found that approximately 40% of reactions to lanolin were nonreproducible; nonreproducibility with other antigens ranged from 20% for nickel to 60% for formaldehyde.⁴⁴

Allergens in Lanolin

Researchers have been investigating antigenic compounds in lanolin for more than 50 years. Although no specific antigens have been determined, most researchers agree that any such allergen (or allergens) resides in the alcoholic fraction produced by the hydrolysis of lanolin.^{6,48,49} Sulzberger and Lazar were the first to report this in 1950. In their study, four patients with previous allergic reactions to lanolin were tested with 12 different lanolin-related substances, including lanolin fatty acids, mixed lanolin alcohols, two types of lanosterol, two types of cholesterol, and three different commercial brands of lanolin. The fractions containing the mixed lanolin alcohols were the only substances that elicited a reaction in all subjects.⁵⁰ Three years later, Sulzberger and colleagues tested 19 lanolin-sensitive patients to one or more of 16 different lanolin products, including cholesterol, mixed lanolin alcohols, aliphatic alcohol fraction, cetyl alcohol, mixed lanolin fatty acids, and combined lanolin fatty acids and alcohols. Of the substances tested, the fraction containing the combination of lanolin alcohols and lanolin fatty acids elicited a positive reaction in 18 (94.7%) of 19 individuals tested. Mixed lanolin alcohols (5% in olive oil) produced a response in 16 (84.2%) of 19 patients, and reactions to the aliphatic alcohol fraction (5% in olive oil) were positive in 14 (77.7%) of 18 subjects.

The fatty acids (5% in olive oil) caused positive patch-test results in only 15.7% of the subjects, and other substances tested showed similarly low rates.²⁶

More evidence pointing toward the alcoholic fraction of lanolin as the sensitizing agent came in 1968 from De Beukelaar, who tested three patients with suspected reactions to Eucerit, which contains wool fat-alcohol fractions and petrolatum. When water is added to this mixture, the resulting commercial product is known as Aquaphor (Beiersdorf). These patients were patch-tested with cholesterol, ional (not further characterized), and wool fat-alcohol fractions A and B, in addition to Eucerit. The common elicitor in all patients was fraction B of the wool fat-alcohols. One patient had positive reactions to Eucerit, both wool fat-alcohol fractions, and cholesterol, which led the author to postulate that the culprit may lie within cholesterol, an oxidation product of cholesterol, or possibly one of those products reacting with the alcohol fraction.⁵¹ Ellis was the first to propose the idea that cholesterol in lanolin may be the cause of contact dermatitis from lanolin, 21 years before De Beukelaar made this claim.⁵²

Other studies have indicated that a mixture of sterols may be more important than different fractions of lanolin alcohols. In a report by Oleffe and colleagues in 1978, of 30 subjects tested, 23 reacted to mixed sterols while only 16 and 14 showed positive reactions to mixtures A and B of lanolin alcohols, respectively.⁵³ All were criticized by Kligman for the unlikelihood that cholesterol or any mixture of sterols could cause lanolin allergy.² In a guinea pig maximization test, two sterol-like fractions were unable to induce sensitization whereas the methylated alcohol fraction of lanolin was able to sensitize 10 to 30% of 10 animals.⁵⁴

The fatty acid fraction of lanolin has also been implicated as a sensitizer, by Sulzberger and colleagues. In their previously mentioned study, they were successful in eliciting positive patch-test results in 2 of 19 patients who had been previously regarded as "lanolin sensitive." This rate, however, is much lower than the rates found for alcoholic fractions.²⁶

Pesticide residues in lanolin may result from either "dipping" sheep in various pesticides to control external parasites or from ingestion of grass containing pesticides.^{55,56} In the late 1980s, several published reports implicated these residues as a source of sensitization.⁵⁷⁻⁵⁹ However, a comprehensive literature search did not yield any studies specifically evaluating the allergenic potential of pesticides in lanolin.

Hypersensitivity to hydrogenated lanolin was first described by Vollum in 1969.⁶⁰ Sugai and Higashi became

interested in hydrogenated lanolin after dermatitis from an ointment containing hydrogenated lanolin increased in Japan in the early 1970s. It was originally suspected that hydrogenated lanolin would be less sensitizing than hydrous lanolin. However, their study found that among dermatitis patients, 38 (5%) of 756 reacted to hydrogenated lanolins whereas only 2.8% (21 of 756) reacted to anhydrous lanolin. It is possible that the products of hydrogenation were allergenic or that contamination with other allergens (such as nickel, copper, and chromium) during the hydrogenation process could have affected reactivity.⁶¹

It is well established that some samples of lanolin and its derivatives may produce a positive reaction whereas others will not.^{28,62,63} In Denmark, Hjorth and Trolle-Lassen tested "fresh" and "old" (ie, stored in a tight jar for 7 years) Eucerin (not further specified) in 20 lanolin-sensitive patients; 11 of the 20 patients reacted positively to fresh lanolin whereas all reacted to old lanolin, suggesting that oxidation products may be antigenic.²⁸ This provides some evidence for oxidation products as antigens; however, larger study populations are needed to further investigate the relevance of these reactions.

The "Lanolin Paradox"

In 1996, Wolf used the term "lanolin paradox" to describe four clinical phenomena.⁶⁴ The first two were similar to those outlined by Fisher for parabens ("paraben paradoxes"): (1) medicaments containing lanolin can sensitize patients, especially those with eczema, whereas lanolin-containing cosmetics are generally less sensitizing; and (2) lanolin-containing medicaments can cause an allergic contact dermatitis when applied to ulcerated skin, but those same patients will not develop a reaction to lanolin-containing cosmetics. Wolf reasoned that lanolin is a weak sensitizer in normal skin whereas damaged skin is easily sensitized. The third lanolin paradox is that lanolin-sensitive patients often have negative patch-test reactions to pure lanolin; this may be due to a low concentration of allergens. As the fourth paradox, Wolf concluded that just as Fisher stated that using only a paraben mix is not a reliable method to test for paraben allergy, the use of only 30% wool alcohols to test for allergy to lanolin is insufficient^{64,65}

Patch Testing

When used "as is," lanolin is thought to be a weak allergen. This raises concern that using pure lanolin in patch tests may produce many false-negative reactions.^{1,28} Early dermatologists experimented with different methods,

using lanolin, eucerin, and varying concentrations of wool alcohols with or without the addition of keratolytics.^{1,26-28,66-68} Since the late 1960s, 30% wool alcohols have been advocated as the standard for patch testing.³²

The use of more than one patch-testing substance for detecting lanolin allergy is important, and the use of AL-101 (100%) has been reported to cause fewer irritant reactions. Mortenson tested 899 patients undergoing patch testing with wool alcohols, hydrogenated lanolin, Eucerin, and AL-101. Of those tested, 6.7% were positive to at least one of these allergens; approximately half of these would have been missed if only wool alcohols had been used.³⁰ More evidence for the use of AL-101 in patch-testing came out of a 1997 Belgian study. Matthieu and Dockx reported two groups of patients with dermatitis who were tested with a standard series containing wool alcohols (30% pet) and AL-101 (100%). In the first group, 45 (11.5%) of 393 patients had positive reactions to wool alcohols or AL-101 (100%) or both: 32 reacted to only AL-101 (100%), 1 reacted to only wool alcohol, and 12 reacted to both. The second group was tested with wool alcohol (30% pet), AL-101 (100%), and AL-101 (50%). Of the 28 patients who reacted to at least one of these compounds, 9 reacted only to AL-101 (100%), 8 reacted only to AL-101 (50%), 5 reacted to both the 50% and 100% concentrations of AL-101, 1 reacted to only wool alcohol, and one reacted to both wool alcohol and AL-101 (100%) (results for the remaining 4 patients were not reported).³²

In the 1989 Swedish study by Edman and Moller, 33 patients with previously reported positive patch-test reactions to wool alcohols, AL-101, or both were retested with wool alcohols (30% pet); AL-101 (as is); Ameralk (Amerchol), the alcoholic fraction of AL-101 (7% pet); white petrolatum; Decubal cream (Alpharma, Bridgewater, NJ) (as is); and Golden Fleece (Alpharma), a form of purified anhydrous lanolin found at a concentration of 6% in Decubal. Twenty-five percent of these patients would have been missed if only 30% wool alcohols or AL-101 had been used whereas only 10% would have been missed if both AL-101 and wool alcohols had been used. Of the six test substances used, Ameralk caused positive reactions in 85% of the 20 patients who had positive reactions to the lanolin products.⁴² Currently, most patch-test experts use both 30% wool alcohols and AL-101 for the detection of lanolin allergy.

“Hypoallergenic” Lanolin

Hjorth and Trolle-Lassen hypothesized that the use of antioxidants may stabilize possible allergens and reduce

the allergenicity of lanolin. They patch-tested 13 patients found previously to have positive reactions to lanolin with anhydrous lanolin, salicylic acid (5%) in lanolin, and three different preparations of lanolin plus antioxidants (2% p-aminophenol, 5% pyrogallol, 2% p-phenylenediamine). All 13 subjects had positive reactions to both antioxidant-free lanolin preparations whereas only 3 of the 13 reacted to p-aminophenol in lanolin. No patients reacted to pyrogallol or p-phenylenediamine in lanolin. Importantly, all three of these antioxidants are known contact allergens. To our knowledge, these antioxidants have not been used in commercial lanolin products to decrease sensitization rates.²⁸

In 1981, Clark and colleagues showed that reducing the free alcohol content of lanolin decreased its sensitizing potential. A large portion of the free alcohols and most of the detergent were removed from anhydrous lanolin. Thirty-four patients previously found to be “lanolin sensitive” were patch-tested with the purified lanolin. When the free alcohol content of lanolin was reduced to 1.5% and the detergent content was reduced to 0.01%, there were no positive reactions. Subsequently, these same 34 individuals were then retested with sequentially higher concentrations of free alcohols. Concentrations of 5% wool alcohols yielded positive reactions in 41% of subjects while 59% reacted to 10% wool alcohols. Increasing the alcohol content to 20% and 30%, however, did not significantly further increase the positive rate (64% and 59%, respectively). Detergent concentrations of 0.05%, 0.15% and 0.3% added to the wool alcohols (10% pet) product resulted in positive reactions in 50%, 50% and 55% of those patients, respectively, and indicated a nonsignificant effect of detergent. In addition, Clark and colleagues summarized eight different series of patch tests with reduced-alcohol-content lanolin. No sources were cited, and specific information about previous lanolin sensitivity and exact concentrations of lanolin alcohol were not reported. However, they stated that among 149 subjects tested with reduced-alcohol-content lanolin in four different clinics, there was “an overall reduction in incidence (of positive reactions) of 99.3%.” They suggested that if pharmaceutical companies limited the free alcohol content of lanolin in topical medicaments to 3% or less, the number of patients sensitized to lanolin would be greatly reduced.⁶⁹

Medical-grade lanolins are thought to be much less antigenic than less purified forms of lanolin. Medilan (Croda, Yorkshire, UK) is a medical grade of highly purified lanolin. It is made through a process of extraction and distillation, which removes all detergents and reduces

free alcohols to less than 3%. The pesticide residue in Medilan is less than 1 mg/kg.⁷⁰ Morris and colleagues tested 27 AL-101-sensitive patients with Medilan; only one (3.7%) reacted.⁷¹ In 2002, Ardern-Jones and colleagues conducted a three-part study to evaluate allergic contact dermatitis from four types of Medilan. The first group consisted of 61 patients, including 24 atopic individuals and 12 patients with varicose eczema or leg ulcers. The second group consisted of 50 patients with chronic leg ulcers, and the third group consisted of 6 patients who had been previously classified as lanolin sensitive (positive patch-test reactions to 30% wool alcohols). No patient in any of the groups showed a reaction to the four Medilan preparations.⁷²

Summary

Lanolin is a common component of consumer products. The potential benefits of this renewable resource deserve careful consideration. Whereas allergic contact dermatitis from lanolin and its derivatives was thought previously to be common, recent reports now show it to be less so. High-risk populations include those with chronic dermatitis, especially venous stasis dermatitis. Dermatologists should therefore reserve a higher suspicion for lanolin allergy in these patients, especially when they present with new onset or worsening of dermatitis while using lanolin-containing products. More research is needed to determine the antigenicity of different lanolin components and the safety of highly refined medical-grade lanolin for use in wool alcohol-sensitive patients as well as for primary prevention of sensitization to lanolin.

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