

Emergent and Unusual Allergens in Cosmetics

David Pascoe, Linda Moreau, and Denis Sasseville

Allergic contact dermatitis from cosmetics is a common problem that is occasionally caused by new or rare allergens. When a patient has a positive patch test to a cosmetic product but to none of the common or commercially available allergens, it is important to further patch-test this patient to the ingredients of the product. Thorough testing with the breakdown of ingredients, usually obtained through cooperation with the manufacturer, often allows identification of the culprit allergen in the cosmetic product. In this article, we discuss emerging or rare allergens discovered by this method, including nail lacquer and lipstick allergens, copolymers, shellac, alkyl glucosides, glycols, protein derivatives, idebenone, and octocrylene.

THROUGHOUT RECORDED HISTORY (and likely before), humans have been altering their appearance to match their social groups' perceptions of beauty or hygiene. The US Food and Drug Administration has stated that "the term 'cosmetic' means (1) articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and (2) articles intended for use as a component of any such articles; except that such term shall not include soap."¹ According to this broad definition, cosmetics are used by the vast majority of people. As the high demand might suggest, a plethora of cosmetics are available for various applications, each with a unique formulation of synthetic or natural ingredients. Exposure to these chemicals can sometimes result in undesirable side effects, including allergic contact dermatitis (ACD) and photocontact dermatitis (PCD). Both can be very distressing for patients, who are often unwilling to stop using all cosmetic products. In recent years, extensive reviews of contact dermatitis from cosmetics have been published, often with lists of recommended allergens for patch testing.²⁻⁵ Patch testing and photopatch testing

can greatly benefit patients by identifying specific allergens, allowing the avoidance of cosmetics that cause ACD and PCD while permitting the use of safe alternatives.

Often, investigating patients for an adverse cutaneous reaction to a cosmetic is straightforward, and the offending allergen is quickly found. However, an important subset of patients will react only to their own products and to none of the allergens from the standard panel or extended series. In-depth patch testing of these patients with the individual ingredients of the formulation is very important, not only for the patients' own benefit but also because patch testing provides new information about emerging allergens that may cause reactions in other individuals. Such new allergens eventually become part of baseline or extended series, and international contact dermatitis panels monitor their allergenic potential. In the United States, the Expert Panel of the Cosmetic Ingredient Review Board analyzes the published literature and regularly publishes safety assessments of cosmetic ingredients. The industry will often respond to the discovery of a significant allergen by removing it from products, and the rate of allergic reactions to it will then decline. For example, the preservative methyl dibromoglutaronitrile was banned in the European Union countries first from stay-on products and later from rinse-off cosmetics because of increasing rates of contact allergy.⁶ The effect of such legislation has been a decrease in trends of contact allergy to this preservative.⁷

The first part of this review focuses on emerging and rare allergens primarily found in lipsticks and nail lacquers. A more general discussion follows, emphasizing important new and unusual allergens encountered in other types of cosmetics.

From the Department of Dermatology, University of North Carolina-Chapel Hill, Chapel Hill, NC, and the Division of Dermatology, McGill University Health Centre, Royal Victoria Hospital, Montréal, Québec, Canada.

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Methods

Relevant references were obtained through PubMed with the following search words: contact dermatitis, photo-contact dermatitis, allergy, cosmetic, nail lacquer, nail polish, nail varnish, lipstick, lip gloss, lip balm, shampoo, and sunscreen.

We define emergent allergens as those that have been reported during the last decade; these include copolymers, ricinoleic acid derivatives, pentyleneglycol, ethylhexylglycerin, alkyl glucosides, protein derivatives, idebenone, and octocrylene. We also include uncommon allergens that have been reported prior to 2000, such as branched-chain fatty acid esters, shellac, pentaerythritol rosinate, isopalmityl diglyceryl sebacate, and butylene glycol. We have selected for inclusion in this review allergens or families of allergens that have been reported more than once and for which patch-test reactions were deemed relevant; all patients reacted to the cosmetic suspected of causing their dermatitis and to the chemical that was later identified by tests with the individual ingredients of the culprit cosmetic. Our findings are summarized in Table 1.

Nail Lacquer

The first case of ACD from nail lacquer (also called nail polish or nail varnish) was reported as early as 1925.⁸ Today, nail lacquer dermatitis remains a common problem. The classic presentation is an ectopic dermatitis with involvement of the eyelids, face, or neck, but other areas (such as the trunk and genitals) may be affected at times. Painted on as a liquid, a nail lacquer should quickly become a water-insoluble and chip-resistant but flexible solid; for a long time, these required characteristics challenged industrial chemists.

Nail lacquer as we know it is a product of the twentieth century. Its numerous components include (1) solvents that evaporate after application, (2) film-forming polymers such as nitrocellulose, (3) adhesive resins, (4) plasticizers that add flexibility and durability, (5) coloring pigments, and (6) various additives such as guanine, mica, and ground fish scales to create "pearlescence."⁸ A basecoat contains more resin (for enhanced adherence to the nail plate) while a topcoat contains more nitrocellulose (for increased shininess).⁹

The most common allergen in nail lacquer is tosylamide formaldehyde resin (TSFR), formerly known as toluenesulfonamide formaldehyde resin. Even when polymerized and solid, this resin still emits allergenic water-soluble monomers and dimers that are responsible

for ACD.⁸ Additional allergens in nail lacquer include formaldehyde, ethylene dichloride, phthalates, guanine, methyl methacrylate, epoxy resin, nitrocellulose, polyester resin, amyl acetate, and butyl acetate.^{8–14}

More recently, some publications have identified copolymers as new and unexpected allergens in nail lacquers. Polymers are structures made by linking together smaller components, or monomers. When a molecule is constructed of two different monomers, it is called a copolymer or heteropolymer.¹⁵ Copolymers are often large molecules with high molecular weights and are used as antistatic, viscosity-increasing, and emulsion-stabilizing agents. Their film-forming properties make them highly suitable for use in nail lacquers. It is believed that impurities, by-products, or degradation products are responsible for ACD because copolymers, due to their large size, are unlikely to behave as haptens.¹⁵

Since 2002, eight cases of ACD from copolymers in nail lacquers have been reported; all of the patients reacted to phthalic anhydride/trimellitic anhydride/glycols copolymer.^{16–18} Seven patients presented with dermatitis involving the head and neck, three additionally had eczema of the fingers or onychodystrophy, and one suffered from periungual dermatitis only. All had been tested with their own nail lacquers, with positive results. The allergen was identified by further retesting with a breakdown of individual ingredients provided by the manufacturers. Of importance, all patients who were patch-tested had negative reactions to TSFR. Two of these patients were further patch-tested with phthalic anhydride, trimellitic anhydride, and glycol monomer, with negative results. This suggests that (as is the case with TSFR) the water-soluble by-products of the hardened polymer causes the ACD.

Lipstick

In contrast to that of nail lacquer, the composition of lipstick appears to be quite simple. A wax is needed to hold the shape of the lipstick and provide ease of application. The wax is usually beeswax, carnauba wax, or candelilla wax, the latter two being plant extracts.¹⁹ Various D&C dyes and inorganic pigments such as titanium dioxide supply the color, and an oily base is required to suspend the pigment. Additives (such as emollients), antioxidants (such as gallates), and sunscreens are also present, each carrying a potential risk for ACD.^{20–22} Among dyes, eosin was formerly a notorious allergen and is now rarely used. However, D&C yellow 11 and D&C red 7 have reportedly caused allergic cheilitis.^{23,24}

Table 1. Overview of Allergens in Cosmetic Products

<i>Product Type</i>	<i>Allergen</i>	<i>Pts</i>	<i>Location of Dermatitis</i>	<i>Age (yr)</i>	<i>Sex</i>	<i>Country</i>	<i>Reference</i>
Nail lacquer	Phthalic anhydride/trimellitic anhydride/glycols copolymer	1	Face	33	F	UK	16
Nail lacquer	Phthalic anhydride/trimellitic anhydride/glycols copolymer	4	Fingers (3/4), face (3/4)	21, 22, 33, 55	F	UK	17
Nail lacquer	Phthalic anhydride/trimellitic anhydride/glycols copolymer	3	Fingers (1/3), face (3/3)	20, 53, 57	F	France	18
Lipstick	D&C yellow 11	1	Lips	38	F	Canada	23
Lipstick	D&C red 7	1	Lips	26	F	Korea	24
Lipstick	Propylene glycol ricinoleate	1	Lips	28	F	Japan	26
Lipstick	Unknown, but sensitized to ricinoleic acid	1	Lips	30	F	China	27
Lipstick, deodorant	Zinc ricinoleate/glyceryl ricinoleate	1	Lips, axillae, arms	51	F	Germany	28
Lipstick	Diisostearyl malate/glyceryl diisostearate	1	Lips	18	F	Japan	29
Lipstick	Diisostearyl malate	3	Lips	27, 20, 29	F	Japan	30
Lipstick	Diisostearyl malate	1	Lips	18	F	USA	31
Lipstick	Glyceryl monoisostearate monomyristate	1	Lips	23	F	Japan	32
Lipstick, “anticellulite” cream	Isononyl isononanoate	1	Lips (NA for cream)	40	F	Belgium	33
Cream	Cetearyl isononanoate	1	Legs	23	F	France	34
Lipstick	Isopalmityl diglyceryl sebacate	1	Lips	27	F	Japan	35
Lipstick	Isopalmityl diglyceryl sebacate	1	Lips	17	F	Japan	36
Lipstick	Isopalmityl diglyceryl sebacate	2	Lips	33, 53	F	Japan	37
Lipstick	Isopalmityl diglyceryl sebacate	2	Lips	35, 41	F	Japan	38
Lipstick, cream	Isopalmityl diglyceryl sebacate	4	Lips (4/4), face (1/4)	27, 32, 50, 46	F	Japan	39
Lipstick	Pentaerythritol rosinate	1	Lips	33	F	Japan	37
Lipstick	Pentaerythritol rosinate	1	Lips	24	F	Japan	40
Lipstick	Pentaerythritol rosinate	1	Lips	27	F	Japan	41
Lipstick	Shellac	1	Lips	20	F	UK	42
Lip care products	Shellac	5	Lips	22–49	F	UK	43
Epilating cream	PEG-22/dodecyl glycol copolymer	19	Primarily severe folliculitis	16–42	NA	Belgium, France	44
Epilating cream	PEG-17/dodecyl glycol copolymer	5	Primarily severe folliculitis	26–32	NA	Belgium, France	44
Moisturizing milk	PEG-17/dodecyl glycol copolymer	1	Extremities	43	F	France	45
Cream	VP/eicosene copolymer	1	Hands, extremities	59	M	Italy	46
Sunblock	VP/eicosene copolymer	1	Face	32	F	UK	47
Sunblock	VP/eicosene copolymer	1	Face	34	F	France	48
Sunblock	PVP/1-triacontene copolymer	1	NA	3	F	UK	49
Spray moisturizer	PVP/hexadecene copolymer	1	Face, legs, trunk	53	F	USA	50
Spray moisturizer	PVP/hexadecene copolymer	1	Extremities	52	F	USA	51
NA	PVP/hexadecene copolymer	1	NA	NA	NA	NA	52
Mascara	Shellac	5	Eyelids	17–34	F	France	53
Mascara	Shellac	1	Eyelids	29	F	USA	54
Mascara	Shellac	1	Eyelids	41	F	Italy	55
Shampoo, sunblock	Decyl glucoside	4	Hands, extremities	16, 52, 53, NA	F	Belgium	56
Antiseptic gel	Decyl glucoside	1	Abdomen	29	F	France	57
Sunblock	Decyl glucoside	1	Trunk, extremities	67	M	Belgium	58
Body and cleaning lotions, sunblock	Lauryl glucoside, coco glucoside	1	Hands	46	F	Belgium	59

Table 1. Continued

<i>Product Type</i>	<i>Allergen</i>	<i>Pts</i>	<i>Location of Dermatitis</i>	<i>Age (yr)</i>	<i>Sex</i>	<i>Country</i>	<i>Reference</i>
Hair mousse	Decyl glucoside	1	Scalp, chest, back, neck, face	25	F	UK	60
Sunblock	Decyl glucoside	1	Face	36	F	France	61
Facial cream	1,3-Butylene glycol	1	Face (erythematous papules)	60	F	Japan	62
Creams, lipsticks, foundation	1,3-Butylene glycol	9	NA	20–58	F	Japan	63
Creams, lotions, milks	1,3-Butylene glycol	1	Face, neck	63	F	Japan	64
Supertanner	1,3-Butylene glycol	2	Face, body	21, 25	F	Belgium	65
Cream	Pentylene glycol	1	Groin, axillae	39	M	Italy	66
Cream	Pentylene glycol	1	Hands, body	44	F	USA	67
Cream	Pentylene glycol	1	Face	56	F	Belgium	68
Cream	Ethylhexylglycerin	1	Face	57	F	Belgium	69
Sunblock	Ethylhexylglycerin	1	Face, arms, hands	64	F	Denmark	70
Creams	Hydrolyzed wheat proteins	1	Contact urticaria	46	F	France	72
Cream	Hydrolyzed wheat proteins	1	Contact urticaria	27	F	Finland	73
Creams, hair products, gels	Hydrolyzed wheat proteins	8	Contact urticaria	21–53	NA	France	74
Cream	Hydrolyzed wheat proteins	1	Eyelids, face, neck	64	F	Spain	75
Cream	Hydrolyzed wheat proteins	1	Scalp, face, neck	42	F	UK	76
Cream	Oat extract	1	Arms, hands	3	F	Italy	77
Cream	Soybean extract	1	Face	55	F	UK	78
Anti-aging cream	Idebenone	1	Face	47	F	Canada	79
Anti-aging cream	Idebenone	1	Face, neck	43	F	UK	80
Anti-aging cream	Idebenone	1	Face	50	F	UK	81
Sunblock	Octocrylene	2	Where applied	31, 55	M	France	83
Sunblock	Octocrylene	2	Where applied	3, 10	M	Italy	84
Sunblock	Octocrylene	2	Where applied	7, 48	F, M	Belgium	85
Sunblock	Octocrylene	12	NA	NA	M (6), F (6)	France	86

F = female; M = male; NA = data not available; PEG = polyethylene glycol; Pts = patients; PVP = polyvinylpyrrolidone; UK = United Kingdom; VP = vinylpyrrolidone.

Ricinoleic Acid Derivatives

Castor oil, also known as ricinus oil, is a pale yellow, viscous, flammable, and indigestible oil that has long been an important base in lipstick production. It is a triglyceride whose fatty acids are largely ricinoleic acid. It has a very high viscosity, and most pigments are soluble in it. It can be found in lipsticks, makeup, nail lacquer removers, lotions, moisturizers, and soaps. Allergic reactions, which are likely due to free ricinoleic acid, have been reported many times.²⁵

Newer formulations that contain ricinoleic acid in structures other than triglycerides have also been found to cause ACD. Propylene glycol ricinoleate, a monoricinoleate of propylene glycol, caused ACD in a 28-year-old woman from Japan. The patient showed no reaction to

propylene glycol; therefore, it was believed the reaction was secondary to ricinoleic acid.²⁶ Another woman had a 1-year history of pigmented ACD of her lips, which was found to be secondary to ricinoleic acid although the exact composition of the lipstick she purchased from her general practitioner was unknown. After she stopped using the lipstick, she had a complete resolution of pruritus but only a 40% improvement of the lip hyperpigmentation after 1 year. Of interest, her patch-test reaction to the lipstick also was hyperpigmented.²⁷ A third woman became sensitized to zinc ricinoleate from a new deodorant; afterwards, she was unable to use the lipstick that she had worn and tolerated for many years and which contained glyceryl ricinoleate. She cross-reacted to sulfated castor oil but not to castor oil itself.²⁸

Branched-Chain Fatty Acid Esters

Five patients have been reported with ACD from diisostearyl malate, a branched C₁₈ aliphatic compound. It is a common ingredient in lipsticks, foundations, blushes, eye shadows, creams, and hair conditioners but is present in much higher concentrations in lipsticks than in other cosmetic products. The first report of a case of ACD from diisostearyl malate was published in 1987. An 18-year-old Japanese woman presented with acute erythematous and vesicular lip dermatitis. Patch testing gave positive results for her lipstick as well as for two of the ingredients, glyceryl diisostearate and diisostearyl malate. These are both C₁₈ aliphatic compounds and differ only in their branching points.²⁹ A more recent Japanese case series report described three women with patch test-proven allergic cheilitis that resolved with discontinuation of the exposure.³⁰ An 18-year-old woman in the United States had a similar reaction.³¹ Glyceryl monoisostearate monomyristate, another branched-chain fatty acid ester, also caused ACD in a 23-year-old woman from Japan.³²

Goossens and colleagues recently reported a case of allergic cheilitis caused by isononyl isononanoate in Rouge Novalip lipstick (Laboratoires La Roche-Posay, La Roche-Posay, France). This patient also reacted to the “anti-cellulite” cream Roc Retinol Body Contouring Triple Action Crème (Johnson & Johnson, Issy-les-Moulineaux, France), which contained the same ingredient.³³ Previously, Le Coz and Bressieux described a case of ACD from the related chemical cetearyl isononanoate.³⁴

Isopalmityl Diglycerol Sebacate

Because branched-chain fatty acid esters can cause lip dryness, isopalmityl diglycerol sebacate (DGS) was developed in Japan in 1994 for use as a lipstick base. As does castor oil, DGS has hygroscopic (water-holding and water-releasing) properties. It is composed of isopalmitic acid, the hydroxyl radical of diglycerin, and sebacate. Cosmetics that contain DGS are produced in Japan and exported to Korea and Taiwan.

The first report of ACD from DGS was published in 1999. A 27-year-old Japanese woman experienced desquamation and swelling of her lips within a month of using a new lipstick. She reacted only to the lipstick on the initial patch test and only to DGS when retested with the lipstick's individual ingredients. Upon discontinuation of the lipstick, her symptoms resolved.³⁵ The same issue of *Contact Dermatitis* contained a report of a 17-year-old Japanese woman who had allergic contact cheilitis and

who reacted to the DGS oligomer. Upon further testing, however, she reacted to isopalmitate alone but not the diglycerol or sebacic acid fractions, and her sensitization was believed to be secondary to isopalmitate.³⁶

By 2003, eight cases had been reported (not including that of the patient whose reaction was attributed to isopalmitate). Sensitization occurred after 2 weeks to several years of exposure.^{37,38} Four more cases were reported in Japan in 2006, and one of these patients had a facial dermatitis in addition to lip dermatitis because she had used a facial cream that also contained DGS.³⁹ As the molecule is very large, it is unlikely that DGS is the primary antigen. As with TSFR, investigators suspect a smaller-molecular-weight degradation product or by-product to be the culprit.³⁸ Certainly, isopalmate is a candidate.

Pentaerythritol Rosinate

Pentaerythritol rosinate (PER), an ester gum derived from colophony, has caused ACD in three patients. A 33-year-old woman in Japan suffered from allergic cheilitis from a lipstick and had a positive patch-test reaction to both PER and DGS.³⁷ Another woman with ACD from her lipstick was found to be allergic to both ricinoleic acid (likely from castor oil) and PER.⁴⁰ There has been only one case report of a patient's being exclusively allergic to PER; she did not cross-react to rosin, abietic acid, *Myroxylon pereirae*, or ester gum.⁴¹

Shellac

Shellac, also known as lacca or gomme-laque, is the resin secreted by the female of the insect *Laccifer (Tachardia) lacca*. This viscous gummy resin hardens to form a substance called lac. Lac is used as a protective shell for the insect's larvae and is harvested from trees. For human uses, lac is crushed, washed, dried, chemically refined, and then drawn into thick sheets called shellac. Shellac or its wax has many cosmetic uses and is found in pump or aerosol hair sprays, shampoos, eyeliners, mascaras, nail lacquers, and lipsticks. Shellac contains many chemicals that vary depending on its chemical processing, season of harvesting, and geographic source. It is recommended to patch-test shellac at a concentration of 20% in ethyl alcohol because the raw material is irritating and tends to form shards when ground.

The first report of ACD from shellac was published in 1986. A 20-year-old woman had a 6-month history of cracking and swelling of both lips and was sensitized to

shellac, lanpol 5 (a polyethoxylated lanolin containing small amounts of lanolin alcohol), and colophony.⁴² In 2001, Orton and colleagues published a case series on five patients with ACD from shellac in lipstick.⁴³ In most cases, the reaction persisted for some time after the withdrawal of the offending agent. Data from these series were limited, but cosensitization with colophony was present in two patients.⁴³

Other Products

There are many other forms of cosmetics, including shampoos, toiletry products, moisturizing creams and lotions, and perfumes. Although fragrances and preservatives remain the most common allergens in cosmetics, ADC has also been caused by surfactants, emulsifiers, stabilizers, and sunscreens. Given their versatility, it is not surprising to find in different cosmetic formulations some of the allergens previously described in regard to nail lacquers and lipsticks.

Copolymers

Copolymers are found in many products besides nail lacquers. In their comprehensive review, Quartier and colleagues reported that, of approximately 200 copolymers used in cosmetics, seven have caused ACD.¹⁵ Among these are methoxy polyethylene glycol 17 (PEG-17) and methoxy polyethylene glycol 22 (PEG-22) dodecyl glycol copolymers, which were responsible for an epidemic of ACD in 33 patients. The patients had all used Veet (Reckitt Benckiser, Massy, France), an epilating system using warm wax and a soothing moist towel. ACD in these patients presented as a follicular eruption on the legs, which spread to other body parts in two-thirds of patients. Twelve patients were given systemic corticosteroids, and several patients were hospitalized.⁴⁴ Of the 26 patients who were patch-tested during this outbreak, 21 were tested with the PEG-22 dodecyl glycol copolymer, one of the ingredients of the moist towel; 19 of these patients had a positive reaction. Five of 7 patients tested with PEG-17 also had a positive patch-test reaction, and there was significant cosensitization. In another case report, a patient exposed to PEG-17 dodecyl glycol polymer in moisturizing milk developed an eczematous ACD of the limbs and forearms.⁴⁵

Polyvinylpyrrolidone (PVP)/eicosene copolymer in the widely used emollient cream Lipikar Baume (Laboratoires La Roche-Posay) has caused a generalized eruption.⁴⁶ It also has led to facial eczema in several patients after sunblock use.^{47,48} In these preparations, the function of the

copolymer is to enhance water resistance. PVP/eicosene copolymer is also found in other cosmetics, such as mascaras and foundations; however, ACD has not yet been seen in this context.

Related copolymers such as PVP/1-triacontene have caused similar reactions.⁴⁹ The literature contains two reports of ACD from PVP/hexadecene copolymer contained in the body oil Rainbath Oil (Neutrogena, Los Angeles, CA)^{50,51} and one report of ACD from this copolymer in an unspecified skin care product.⁵²

Polyvinyl methyl/maleic acid copolymer (Gantrez, International Specialty Products, Wayne, NJ) has excellent tackifying and adhesive properties and is used in toothpastes, mouthwashes, denture fixatives, and skin care products. However, the three reported cases of ACD were not due to cosmetics but to peristomal adhesive pastes.¹⁵

Shellac

Shellac in mascara can also cause eyelid dermatitis. In a case series of six patients from France, all six had used Great Lash Ultra Noir mascara (Gemey, Clichy, France, and Maybelline, New York, NY), and 5 of 5 patients who were patch-tested with shellac had positive reactions. (The sixth patient could not be tested with the individual ingredients of the mascara.)⁵³ One case of ACD from shellac in mascara in a 29-year-old woman was reported from the United States, but the particular brand of mascara was not mentioned.⁵⁴ A similar reaction occurred in a 41-year-old woman from Italy who used Diorshow mascara (Christian Dior, Paris, France).⁵⁵

Alkyl Glucosides

Glucosides are the condensation products of fatty alcohols, often extracted from palm or coconut oil with glucose. Although originally used in the 1960s as mild non-ionic surfactants in rinse-off products, glucosides fell out of favor and were replaced by newer molecules. They have been making a comeback since the 1990s and, because of their nonirritant potential, are now increasingly used in rinse-off products (ie, shampoos, soaps, cleansers, hair dyes, and even surgical disinfectants) but also in leave-on products such as lotions, creams, fragrances, sunscreens, and tanning products.^{56,57} Glucosides are chemically closely related to other surfactants, such as methyl glucose dioleate, with which they may cross-react. As well, cross-reactions with other alkyl glucosides such as coco glucoside or lauryl glucoside are likely.^{57,58}

At least 10 cases of ACD from aryl glucoside have been described in the literature to date, and eight of these patients were allergic to decyl glucoside.^{56–61} It appears that shampoos are the most common culprits. Involvement of the scalp as well as areas touched by the hair, including the back, chest, and shoulders, is common.⁶⁰ The hands are also involved as they come into contact with the product during application.⁵⁹ In an occupational setting, hair-dressers may develop hand dermatitis.⁵⁶ There was also a severe case of facial ACD that was caused by decyl glucoside in a sunscreen and that required treatment with oral steroids.⁶¹ To date, all sunscreen products that are associated with sensitization to decyl glucoside contain the ultraviolet light absorber Tinosorb M (Ciba, Basel, Switzerland). This physicochemical sunscreen contains decyl glucoside as a stabilizer of its microfine particles.

Glycols

Glycols are aliphatic dialcohols often used as solvents, preservatives, and humectants in cosmetic products. The prototype of this class, propylene glycol (PG), is believed to have more allergic potential than newer related molecules. However, evidence is emerging that the new PG derivatives cause ACD as well.

In the early 1990s, three cases of ACD from 1,3-butylene glycol (1,3-BG) were reported in the Japanese literature.⁶² In a prospective study conducted at two Japanese centers from 1994 to 1999, 9 of 758 patients had ACD from 1,3-BG. In each of these cases, 1,3-BG was found in a cosmetic product, most commonly in creams and lotions but also in hair dyes and lipsticks. Of importance, only one patient had a cross-reaction with PG. Irritant reactions were also noted in four patients.⁶³ ACD from 1,3-BG continues to be a problem in Japan; in 2003, a case of ACD from 1,3-BG along with simultaneous sensitization to trisodium hydroxyethyl ethylenediamine triacetate was reported.⁶⁴ In 2000, a report from Belgium described generalized eruptions in two patients who used a “supertanner” cream containing 1,3-BG. Both of these reactions were brisk, and one patient required systemic corticosteroids. Both patients were also patch test negative to PG.⁶⁵ According to the authors of the article, no case of ACD attributable to 1,3-BG has been reported in North America.

Pentylene glycol, a related chemical, has also been responsible for a number of ACD cases. A 39-year-old Italian man developed a brisk ACD after only 2 weeks of treating an axillary and crural dermatitis with an emollient cream containing pentylene glycol. Patch testing yielded

strong reactions to serial dilutions of pentylene glycol down to 0.5% aqueous. This patient was not cosensitized to PG.⁶⁶ Amado and colleagues reported the case of a 44-year-old atopic woman who became sensitized to pentylene glycol in MimyX Cream (Stiefel Laboratories Inc, Coral Gables, FL), also without sensitization to PG.⁶⁷ A 56-year-old woman developed eczematous lesions on the face and eyelids after using Toleriane Riche cream (Laboratoires La Roche-Posay) and Louis Widmer body lotion (Louis Widmer SA, Schlieren, Germany); both products contain pentylene glycol. The patient had a negative patch-test result but a positive repeat open application test result with a 5% aqueous solution of pentylene glycol. She was also patch test positive to PG.⁶⁸

Two case reports described ACD from ethylhexylglycerin (octoxyglycerin), an emollient dialcohol. The first patient, a 57-year-old woman presenting with an 8-month history of facial dermatitis, reacted to her Toleriane facial cream (Laboratoires La Roche-Posay) and to one of its ingredients, ethylhexylglycerin (10% in petrolatum).⁶⁹ The second patient was a 64-year-old atopic woman who experienced summer exacerbations of her dermatitis. Ethylhexylglycerin was present in her Vichy Capital Soleil sunscreen (Laboratoires Vichy, Asnières-sur-Seine, France). Patch tests and repeated open application tests confirmed the sensitization.⁷⁰ Neither of these patients reacted to PG. A recent case report described a 68-year-old woman who developed ACD from both ethylhexylglycerin and pentylene glycol but not from PG.⁷¹

Protein Derivatives

Proteins, most often derived from plants, are common ingredients in cosmetics. Protein derivatives are included in cosmetic creams and (less commonly) in shampoos and conditioners. The most common protein culprit in ACD appears to be hydrolyzed wheat protein (HWP), and it tends to cause immediate hypersensitivity. HWP is obtained from gluten or (less commonly) total flour proteins. Hydrolysis of proteins is done to increase solubility and is accomplished with acids or enzymes.

Isolated case reports have described patients with HWP-induced immediate hypersensitivity.^{72,73} A more recent publication described a case series of nine patients, including one described in one of the aforementioned case reports, who developed contact urticaria from HWP.⁷⁴ All patients had positive prick-test reactions to HWP but not to wheat flour extract. Although some of these patients reacted to oral HWP exposure, none had difficulty with wheat flour that was not hydrolyzed. The same immu-

noglobulin E (IgE) epitopes are present on both native wheat proteins and HWP. It is suggested that the clumping of aggregates of the hydrolyzed protein leads to multi-epitopic entities more suitable for bridging of IgE on mast cells and basophils. Two publications reported delayed-type ACD from HWP in cosmetic creams, citing positive patch-test reactions at day 4 with the cream and a 10% aqueous solution of HWP in the first case.⁷⁵ In the second case, patch-test results were positive at days 2 and 4 with the cream and with a 50% aqueous solution of HWP.⁷⁶

Oats are another rare cause of ACD. A 3-year-old girl with atopic dermatitis developed an exacerbation of her eczema after using a moisturizing cream. When patch-tested, she reacted positively to the oat extract *Avena Rhealba* (Laboratoires Pierre Fabre, Castres, France). Avoidance of the cream resulted in complete regression of her dermatitis.⁷⁷ Another patient had a 5-month history of dermatitis after having applied a facial cream containing a soybean extract. The erythema began hours after she applied the cream, and the swelling typically persisted throughout the following day. She had positive patch-test reactions to the soybean extract. Of interest, she had no symptoms when eating soybeans, and she had a negative serum IgE level to soybean.⁷⁸

Idebenone

Idebenone is a potent antioxidant and a synthetic analog of coenzyme Q₁₀. It has been used orally in the treatment of Alzheimer disease, Friedreich ataxia, cerebrovascular disease, and liver disease. New cosmeceuticals in which idebenone is claimed to neutralize free radicals and reduce wrinkles or other signs of aging are emerging. In the last 2 years, three cases of ACD from idebenone have been reported.

The first case involved a 47-year-old woman who had an anti-aging cream applied at a salon. Within 24 hours, she developed an edematous vesicular dermatitis of the face, ears, and neck, requiring treatment with oral prednisone. Results of patch testing with the standard series of the North American Contact Dermatitis Group and with an extensive cosmetic series were entirely negative; the patient reacted only to the cream. A later patch-testing session with the individual ingredients of the cream showed a +++ reaction to idebenone 0.5% in petrolatum (pet).⁷⁹ The second patient was a 43-year-old woman who developed an itchy eruption at the sites where a new anti-aging cream had been applied 2 days previously. Her dermatitis resolved within 5 days following applications of a topical corticosteroid, and she had

positive patch-test reactions to her cream and to idebenone 0.5% pet.⁸⁰ The last patient, a 50-year-old woman, had a more acute onset of symptoms, with heat and tightness after 4 hours, followed by erythema and periorbital swelling the next day.⁸¹

All three patients had used the antioxidant facial cream Prevenge (Elizabeth Arden, New York, NY, and Allergan, Irvine, CA). The rapidity of onset of these reactions suggests that the patients had been previously sensitized to idebenone. Because two patients claimed that they had had no prior contact with idebenone, it is likely that they had been sensitized by earlier exposure to coenzyme Q₁₀, which has been present in over-the-counter products for more than 10 years.

Octocrylene

With the increasing awareness of the need for ultraviolet filtration, chemical sunscreens have ironically become the most frequent photoallergens, and their importance as contact allergens is also increasing. The most common culprits include benzophenone-3 (oxybenzone), isopropyl methoxy dibenzoylmethane, and butyl methoxy dibenzoylmethane (avobenzone).⁸² Octocrylene (2-ethylhexyl-2-cyano-3,3-diphenylacrylate) is an ultraviolet B-filtering cinnamate that has been increasingly used during the past 10 years. Because of its intrinsic stability, it may prevent the photodegradation of other chemical filters such as avobenzone.

The first report of adverse cutaneous reactions to octocrylene involved two men (one 31 years old and the other 55 years old) who both suffered from PCD and had positive photopatch-test results. In addition, one of them had multiple concomitant photopatch-test reactions, most notably to ketoprofen.⁸³ In another case series, two boys (3 years old and 10 years old) had pruritic erythematous eruptions after sunscreens containing octocrylene were applied. Both had positive patch-test reactions to octocrylene 10% pet. One was photopatch-tested and showed no evidence of photoallergy.⁸⁴ A 7-year-old girl and a 48-year-old man from Belgium have also been reported with ACD and PCD, respectively, from octocrylene. Of note, the man was also allergic to topical ketoprofen and had a positive photopatch-test reaction to this substance.⁸⁵ A more recent series of 12 cases clearly showed the distinction between pediatric and adult cases. Children tend to develop acute ACD, whereas adults are more prone to PCD. Of the 9 adults in this series, only 1 had ACD, 8 had PCD, and all 9 had a past history of photoallergic contact dermatitis from topical ketoprofen.⁸⁶ Time will tell if

cross-reactions between octocrylene and ketoprofen are seen as frequently in North America, where topical ketoprofen is rarely used.

Conclusion

Our review highlights the importance of testing with the patients' own cosmetics. Contrary to work-related products that may be highly corrosive or sensitizing, cosmetics are usually safe for patch testing. Most leave-on products can be applied undiluted under occlusion. Those (such as mascaras or nail polishes) that contain a solvent should be allowed to dry before occlusion to avoid irritant reactions. Rinse-off products such as shampoos and cleansers should be diluted down to about 1% in water or another suitable vehicle and tested on 10 to 20 controls to ensure that they do not retain their irritant potential even at such dilutions. Alternatively, these products can be tested with the "semi-open" patch test developed by Prof. An Goossens: a small drop of the undiluted product is placed on the skin, allowed to dry, and covered with a piece of porous adhesive tape. This technique minimizes the risk of irritant and false-negative patch-test reactions.

Positive test reactions to a cosmetic warrant further exploration. The manufacturer should be contacted and asked to provide the individual ingredients of the product, mixed in petrolatum or water, at the same concentration as in the finished formulation. Patients should be willing to submit to a repeat session of patch testing with the breakdown of the culprit cosmetic to pinpoint the offending substance.

Allergic contact dermatitis from cosmetics is a common problem, and the formulation of cosmetic products is constantly changing. We have described several classes of allergens (in nail lacquers, lipsticks, and other products) that we suspect will continue to increase in importance in the coming years. Constant vigilance by dermatologists and continued cooperation from the cosmetic industry are necessary to respond to these and future allergens as they emerge.

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