

Allergic Contact Dermatitis to Aerosolized Vildagliptin

To the Editor:

Globally, occupational dermatosis contributed to 1.3% of total years lived with disability between 2011 and 2018.¹ Drug-induced allergic contact dermatitis is not uncommon, and we present 2 cases of occupational allergic contact dermatitis to aerosolized vildagliptin, a dipeptidyl-peptidase 4 inhibitor, not yet reported as a cause for air-borne contact dermatitis.

A 29-year-old process technician started work in January 2016. His job involved unwrapping blocks of 25 kg of metformin to be placed into a machine for crushing. He then added in powdered hydroxypropyl cellulose and powdered vildagliptin for mixing into the same machine. Table 1 shows the substances that he handled. His personal protective equipment included a half-face respirator, 3-piece jumpsuit with hood and long sleeves,² and nitrile gloves.³ He was seen in the National Skin Centre for painful itchy facial rash, which came on 4 months into his job. He developed scaly erythematous plaques distributed over the areas of his face that were exposed while working (Fig. 1). Patch test to powdered vildagliptin showed positive results to 1%, 10%, and 50% powdered vildagliptin (Table 1).

A 41-year-old process factory coworker started work in March 2016 in the same factory. He performed the same duties and wore the same protective equipment as patient 1. He devel-

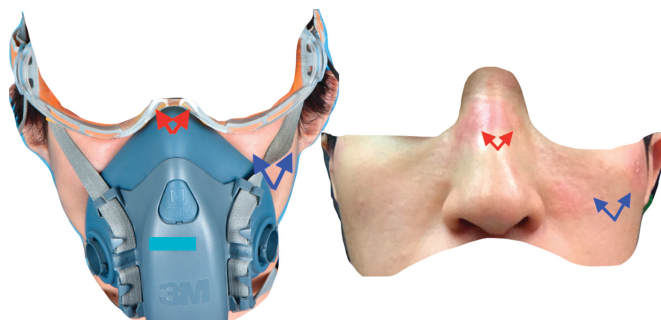


Figure 1. Case 1. Erythematous scaly plaques over exposed areas of face (red and blue arrows).

oped itchy rash over the forearms and face after working 27 months. The findings of examination revealed scaly erythematous plaques over his hands and postinflammatory hyperpigmentation over both cheeks. The findings of patch test showed positive results to 10% and 50% vildagliptin (Table 1).

Vildagliptin has been on the market since April 2010. However, there are no reported cases of allergic contact dermatitis to vildagliptin.⁴ Clues toward a diagnosis of occupational-related air-borne contact dermatitis are location and atypical shape of the rash. These rashes may be mistaken for rosacea or seborrheic dermatitis, but the atypical distribution of the rash outlining the exposed areas where masks or goggles do not cover hints at the diagnosis of possible air-borne contact dermatitis.

The cornerstone of management of air-borne contact dermatitis is elimination of contact with the allergen, but this may be difficult in certain situations. Fortunately, the patients in both cases were reassigned to another department, and their rashes have all resolved. If elimination of contact is not possible, we propose the usage of a comparable alternative, the powdered air-purifying respirator, which would provide adequate protection and respiratory space. Workers should also take care to ensure proper protection during cleaning of a powdered air-purifying respirator, as retained powder on suits can aerosolize.

The impact of occupational contact dermatitis extends from the individual to companies and to health care systems around world. On a national level, this calls for better infrastructure and proper ventilation in manufacturing plants and laboratories to reduce the quantity of aerosolized chemicals that workers come into contact with.⁵ We also propose a concerted effort to collect epidemiologic data of occupation-related allergic contact dermatitis for global surveillance, as these cases are often underreported.

TABLE 1. Patch Test Results

Substance	Patient 1	Patient 2
Metformin powder 1%*†	Negative	Negative
Metformin powder 10%*†	Negative	Negative
Metformin powder 50%*†	Negative	Negative
Vildagliptin powder 1%*†	Positive	Negative
Vildagliptin powder 10%*†	Positive	Positive
Vildagliptin powder 50%*†	Positive	Positive ++
Safety goggle rubber rim	Negative	Negative
3M respiratory rubber rim*	Negative	Negative
Nitrile gloves*	Negative	Negative
Hydroxyl propyl methylcellulose powder*†	Not applicable	Negative
Magnesium stearate powder*†	Not applicable	Negative

*Materials were contained within a small aluminum chamber and secured with Micro-pore tape onto the skin.

†Powdered chemicals were mixed with yellow soft paraffin.

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Undisclosed Fragrance Allergens in Clean Cosmetic Cleansers Place Patients at Risk

In Europe, the Scientific Committee on Consumer Safety requires cosmetic labeling disclosure of 26 of the most common fragrance allergens when included at concentrations known to be allergenic (eg, 100 ppm for rinse-off and 10 ppm for leave-on).¹ While global manufacturers are moving to universally recognize these standards, the choice to use natural sounding names by some companies places patients at risk for contact allergy and additional adverse effects. The publication of prohibited cosmetic ingredient lists in Europe and by non-governmental, governmental, and commercial companies fails to communicate where risk of allergen exposure is possible. Some also reward the use of essential oils and botanicals and recommend avoidance of products that include fragrance or parfum without realizing the former also places patients at risk. A few major retail establishments even use prohibited cosmetic ingredient lists to drive their “clean” cosmetics programs but lack robust scientific evidence to support their choices, often replicating what companies say on their packaging without third-party interpretation and verification. Websites and associations such as SkinSAFE Products

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TABLE 1. Fragrance-, Irritant-, and Allergen-Related Claims by Product

Focused Claim Area	BEB45770	PRC98126	BAB00252	PIP52503	SHE90141	LIV62500	PUR00629	GAI230311	EVE00037	BAJ10171	ORG005013
Clean/pure				X					X		
Free of EW/Gs concerned/1400/2000			X	X					X	X	
left out											
Hypoallergenic											
No allergens/no common allergens		X	X			X					
No fragrances/fragrance		X	X				X				
free/formulated without											
No perfumes											
No skin irritants											
No synthetic fragrance/artificial scents	X										X

(www.skincareproducts.com) and CAMP (the Contact Allergen Management Program) from the American Contact Dermatitis Society are backed by decades of skincare research and help to identify risks of exposure to skin allergens to both professional (SkinSAFE, CAMP) and consumer (SkinSAFE) audiences.

In the present study, 11 consumer cleansing products intended for newborns, infants, children, and people with eczema-prone skin were sourced online and ingredient lists were obtained from manufacturers' websites and package labels for evaluation. Fragrance-related claims were recorded, and ingredients were mapped to nomenclature (INCI) published by the Personal Care Products Council (Table 1; see Supplemental Table 1, available at <http://links.lww.com/DER/A36>; products listed by unique code). To identify ingredients with masking or fragrance/parfum properties, online resources SpecialChem (<https://cosmetics.specialchem.com/>) and INCIDecoder (<https://incidecoder.com/>) were consulted.

Thirty-six percent of products made claims of no fragrance/fragrance free/formulated without fragrance despite containing natural/botanical extracts and essential oils with perfuming, masking, or fragrance functions as listed in INCI, SpecialChem, and INCIDecoder (Table 1). The use of essential oils/botanicals seems to have allowed manufacturers to omit the word “fragrance/parfum” on ingredient lists and hide the fact that these also contain chemicals that would require disclosure per the Scientific Committee on Consumer Safety.¹ Two products additionally made claims of “no allergens/no common allergens” despite containing essential oils with high levels of some of the most common skincare allergens.

Natural oils and botanicals contained in 2 products making claims of no allergens/common allergens (lavender [*Lavandula angustifolia*, *Lavandin*, or *L. officinalis*], tangerine [*Citrus tangerina*], bergamot [*C. aurantium bergamia*], and grapefruit [*C. paradisi*]) have been associated with contact allergy/allergic contact dermatitis.^{2,3} Lavender and tea tree oils are also associated with endocrine-like effects, such as gynecomastia (breast enlargement), in prepubescent boys and girls.^{4–6} This is of particular concern given the unbalanced promotion of essential oils by pseudoscientists who lack the expertise to assess risk and benefit on an individual basis and the lack of awareness of the risks associated with allergen exposure from natural and organic products. Additional research is required to investigate the unintentional adverse effects secondary to essential oil exposure.

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Late Patch Test Reaction to Acrylates in 2 Patients: Should We Schedule a Check at Weeks 2 and 3?

To the Editor:

In recent years, dermatologists have become increasingly interested in allergic contact dermatitis to acrylates. These chemicals are widely used in various industrial settings (plastic, glue, paints), in medicine (dressings, bone cement, dental materials), and in aesthetics, with a particular relevance for nail products.¹ It is now generally recommended to test 2-hydroxyethyl methacrylate 2% in petrolatum (pet.) in standard series.² The aim of our report is to discuss the timing of patch test readings taking a cue from 2 cases of delayed allergic contact dermatitis to acrylates.

Case 1

A 36-year-old woman with atopic dermatitis, asthma, and hand eczema was referred to our patch test clinic. She was a

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Figure 1. Patient 2, 20 days after the patch test showed the persistence of ethyl acrylate 1% in pet. (the lower one) and the occurrence of 2 positive reactions on butyl acrylate 1% in pet. and methyl acrylate 1% in pet. (upper left and right, respectively).

physiotherapist, and sometimes, she applied a long-lasting gel nail. The eczema involved eyelids and dorsal surface of the hands with severe itching. We performed the Italian patch test baseline series (Società Italiana di Dermatologia Allergologica, Professionale ed Ambientale 2016, 29 haptens)² and acrylates series (FINN Chambers Aqua; SmartPractice, Phoenix, Ariz; F.I.R.M.A. S.p.a., Firenze, Italy). On day 4 (D4) and D7, she showed ++ positive reactions to nickel sulfate 5% in pet. and formaldehyde 2% in water. We observed the new appearance of 2 itching round reactions on her back after 10 days; the eczema perfectly matched the area of application of ethyl acrylate 1% in pet. and butyl acrylate 1% in pet.

Case 2

A 69-year-old woman reported a history of 6-month eczema on the eyelids, facial erythema, and itching. Previously, she worked as an employee in a law office, but after retirement, she started painting. The patient reported having itching and erythema in the past where she had applied muscle taping for analgesic purposes. Therefore, we decided to test standard,

rubber, and acrylates series. On D4 and D7, there was a ++ positive reaction to ethyl acrylate 1% in pet. However, 20 days after patch testing, the patient required an urgent examination for the onset of intense itching on her back. We observed the permanence of ethyl acrylate–positive reaction and the occurrence of 2 new ++ positive reactions with erythema, infiltration, and papules corresponding to the place where the butyl acrylate 1% in pet. and methyl acrylate 1% in pet. had been placed (Fig. 1).

The examination after 3 months in both patients showed a complete resolution of the lesions. Dry skin without relevant eczema persisted in patient 1; therefore, we recommended a daily application of moisturizers.

The European Society of Contact Dermatitis recommends patch test reading times at D2, D3 or D4, and D7; for some allergens, such as corticosteroids and antibiotics, to add a reading between D5 and D10 is mandatory.² Teik-Jin Goon et al³ recognized the importance of D7 reading in acrylate patch test, proving that 7% of cases were positive only on D7. In the past, when acrylate allergy afflicted almost only dental workers, a positive reaction was described 5 weeks after a test.⁴ A late patch test reaction is a possible adverse effect of patch testing, in the case of active sensitization. However, many individual (skin permeation, ultraviolet exposure) and chemical factors (anti-inflammatory influence from the allergen, for example) can influence the time of response to the patch test. The study conducted by Isaksson et al⁵ showed that positive test reactions to 2-hydroxyethyl methacrylate 2% in pet. and ethyleneglycol dimethacrylate emerging after 10 days do not automatically imply active sensitization. In our cases, patients had never undergone patch tests before, but they had repeated contact with acrylate sources, suggesting true late-appearing patch test reactions. In conclusion, further studies are needed concerning this topic, but clinicians should be aware that late patch test reactions to acrylates can occur, as is illustrated by our cases.

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