

Allergic contact dermatitis caused by a new insulin pump system containing isobornyl acrylate

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Isobornyl acrylate (IBOA) has been identified as a major culprit allergen in several glucose sensors and insulin pumps during the past few years. Many cases of IBOA-induced allergic contact dermatitis are related to prolonged use of the FreeStyle Libre sensor (Abbott Diabetes Care, Witney, Oxfordshire, UK).^{1–3}

CASE REPORT

We report a case on a 6-year-old boy with diabetes mellitus type 1 and atopic dermatitis who developed allergic contact dermatitis from the Orbit microinfusion set used together with the insulin pump Mylife YpsoPump (Ypsomed AG, Burgdorf, Switzerland), a medical device not previously linked to IBOA contact allergy.

The patient was diagnosed with diabetes on 7 December 2020. Between 11 December and 15 December, he was equipped with the sensor FreeStyle Libre. On 16 December the sensor was exchanged for the continuous glucose monitoring system Dexcom G6 (Dexcom, Inc., San Diego, California). In January 2021, he received the YpsoPump insulin pump. In April 2021, he developed

acute eczema located under the Dexcom G6 device and after another few months a rash appeared underneath the YpsoPump infusion set (Figure 1).

The patient was investigated with patch test that included selected substances from the baseline series and an in-house medical device series. Patch testing was also performed with acetone extracts made from the adhesive patches and plastic support material from the insulin infusion set and sensor. Each material was extracted in acetone in an ultrasonic bath for 5 min. Thereafter, all extracts were evaporated to a final volume of 0.5 ml. Patch tests were applied on the back and left in occlusion for 48 h using IQ Ultimate chambers (Chemotechnique Diagnostics, Vellinge, Sweden). Reactions were read on day (D) 4 and D7. Scoring was performed according to the criteria of the International Contact Dermatitis Group (ICDRG).⁴

At the first reading on D4, the patient had an extreme (++++) reaction to IBOA 0.3% in petrolatum (pet), a strong (++) reaction to IBOA 0.1% in pet, and a weak (+) reaction to IBOA 0.01% in pet, respectively (Figure 1). Doubtful reactions to sesquiterpene lactone mix and alantolactone were observed. Unfortunately, due to illness

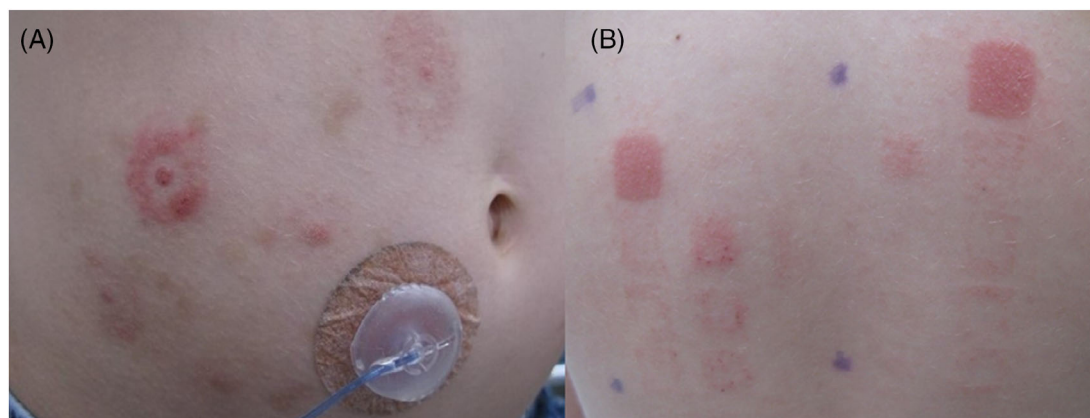


FIGURE 1 (A) Reactions to the infusion set of the YpsoPump (abdomen). (B) Patch test reactions on D4 (upper back). To the left, strong positive reaction to IBOA 0.1% in pet and to the right an extreme positive reaction to IBOA 0.3% in pet. Photographs were taken at test reading on D4.

of a family member, the patient could not appear for test reading on D7. At photographs taken on D7 no new reactions could be identified. However, on D10 a new reaction was observed and photographed by the patient's guardian. When inspecting the photo, the preparation giving the positive reaction was interpreted to be dicyclohexylmethane-4,4'-diisocyanate (DMDI) 1% in pet. The patient's guardian declined further testing.

The extracts of the devices were analysed by gas-chromatography-mass spectrometry (GCMS).⁵ IBOA was found in all four extracts in concentrations corresponding to a total amount of 0.4–0.8 µg IBOA in each material. The surface concentration was 0.02 µg/cm² in the adhesive patch from the infusion set and 0.03 µg/cm² in the adhesive patch from the Dexcom G6 sensor. The GCMS analyses also indicated the presence of DMDI in the extract made from the plastic part of the infusion set.

DISCUSSION

To the best of our knowledge, IBOA content or allergic contact dermatitis related to the YpsoPump insulin pump has not previously been reported. Based on the patient's history and the result from patch tests and chemical investigation it is likely that sensitization was caused by IBOA from the Dexcom G6 glucose sensor or the YpsoPump insulin pump. In previous reports, contact allergy to IBOA in most cases has been associated to prolonged use of FreeStyle Libre sensors,¹ a device our patient had used for only 6 days. Abbott themselves proclaimed the sensors would be IBOA free from 31 July 2020.⁶ Based on this information and our knowledge at date, the patient's FreeStyle Libre sensor most likely contained low levels of IBOA, if any. Therefore, it is highly doubtful that the patient would have been sensitized by this device. Furthermore, dermatitis occurred only first after several months use of Dexcom G6 (April 2021).

In analyses of adhesive patches from early versions of FreeStyle Libre, surface concentrations of IBOA between 0.2 and 6 µg/cm² have been found.^{1,7} As a comparison, our chemical analysis indicates a low quantity of IBOA in both medical devices.

The patient did not show any reactions to the tested adhesive patches nor plastic support material. The clinical picture in this case is most likely explained by the long-term exposure of the medical devices to the skin.

Also contact allergy to DMDI may have contributed to the reaction to the infusion set. As we previously have seen indications of isocyanates being present in diabetes devices,⁸ at the time of testing our medical device series contained isophorone diisocyanate and DMDI. Recently Dendooven et al. have reported on isocyanates as potential allergens in diabetes devices and wound dressings.⁹ In the case reported here the reaction was noticed on D10. Late-appearing patch test reactions may indicate active sensitization. However, patch test reactions to isocyanates are known to sometimes appear late, also after the D7 reading in

sensitized individuals.¹⁰ As the patient's guardian declined further investigation, no supplementary patch testing with DMDI was performed.

The following case report present another insulin pump system added to the list of IBOA-containing medical devices for diabetes management. This case indicates that comparatively low levels of IBOA are enough to sensitize and cause allergic contact dermatitis. Moreover, the case highlights the difficulty of evaluation of clinical relevance as well as to give recommendations about medical devices.

AUTHOR CONTRIBUTIONS

Johanna Enberg: Investigation; writing – original draft; writing – review and editing. **Nils Hamnerius:** Investigation; validation; visualization; writing – review and editing; project administration; supervision; conceptualization. **Martin Mowitz:** Conceptualization; writing – original draft; software; writing – review and editing; project administration; formal analysis; supervision; data curation; methodology; validation; visualization; investigation.

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The patient's guardian has given informed consent to the publication of the case details and photographs.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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Occupational contact sensitization to *Pelargonium zonale* hybrids

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Pelargonium hybrids of the geranium family (Geraniaceae) are popular pot and container plants in many European countries. *Pelargoniums* are often called “geraniums,” although this name is more correctly used for hardy species of another genus. Because of insufficient details in case reports, contact dermatitis from *pelargoniums* is not well documented.¹

CASE REPORT

A 35-year-old atopic female greenhouse worker was referred because of occupational dermatitis of the forearms. The rash appeared after she had handled summer bedding plants, such as dahlias and flowering *pelargoniums*, for a few weeks wearing gloves, and it was accompanied by dyspnea. After discontinuation of the job, she was patch tested in August 2020 with the baseline series, a glove series, geraniol, *Dahlia* oleoresin, Compositae mix II 5% pet. and its constituents as well as leaf and stalk from *Dahlia* and *pelargonium* plants and flower of the latter. The patient had positive reactions to nickel of old relevance and 1+ reactions on day (D) 3 to *pelargonium* leaf wetted with water and ethanol, respectively. Both were negative on D7. Prick tests to standard inhalant allergens were positive to birch and grass pollen and negative to *pelargonium* and *Dahlia*. Histamine release test for *pelargonium* (leaf, flower, stalk) was negative.

After avoiding contact with *pelargoniums*, the patient was re-tested with a *Pelargonium zonale* hybrid from her former nursery in

September 2022 (Figure 1). On D4, she had a follicular, intensely itching reaction to *pelargonium* leaf wetted with water and ethanol, negative on D7. Leaves from the same specimen were tested in 12 controls and elicited absolutely no reactions.

The clinical information above was used after written informed consent from the patient.

DISCUSSION

Pelargoniums, native to South Africa, were introduced to Europe in the 18th century. Although some reports suggested sensitization, Agrup described the leaves as irritant on patch testing.²⁻⁴ This was questioned later by Fregert and Hjorth.⁵ In a Danish study, 4 of 4 gardeners were sensitized and only 1 of 27 controls had a transient doubtful positive reaction on D3.⁶

In the present case, the weak, and over time declining, positive reactions point to a low, but true sensitizing potential in *pelargoniums*. Geraniol is considered the main allergen, but is apparently not the only one.⁷

AUTHOR CONTRIBUTIONS

Evy Paulsen: Conceptualization; investigation; writing – original draft.

Klaus E. Andersen: Conceptualization; investigation; writing – review and editing. **Lone Hvid:** Conceptualization; investigation; writing – review and editing.