Review article

PATCH-TESTING PATIENTS' OWN PRODUCTS: A PRACTICAL OVERVIEW FOR CLINICIANS

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ABSTRACT

Patch tests are the gold standard in the work-up of allergic contact dermatitis. Apart from commercial products, it is also of utmost importance to include the patients' own products. Products with unknown content or containing strong irritant, corrosive, toxic or poisonous chemicals should never be patch-tested, though. Recommendations on how to patch-test finished products can easily be retrieved in the literature and in specialised reference books; practical advice on test modalities (test methods, concentrations, vehicles) have been outlined for leave-on and rinse-off cosmetics, household detergents, chemical products (glues, paints), solid materials (gloves, shoes, textiles, leather goods, metal, plastic and rubber items), occupational products, plants, woods and food items. Separate guidelines exist on how to patch-test drugs. Whenever a positive or negative reaction to a product is obtained, practitioners should always question the possibility of a false-positive or a false-negative reaction, respectively. In these cases, additional test procedures may be required (eg testing of separate ingredients, repeated open-application tests, serial dilutions of a chemical or product, glove-repeated application tests). In this article we provide a practical overview for clinicians on how to test patients' own products.

Keywords: Repeated open-application test (ROAT), semi-open, patch test, prick test, cosmetics, occupational products, allergic contact dermatitis

INTRODUCTION

Patch tests are the gold standard in the work-up of suspected allergic contact dermatitis (ACD). In addition to commercial patch-test preparations, it is essential also to include the patients' own products.[1–2] This is not only to determine the relevance of a positively reacting commercial chemical if it is an ingredient in the product that also resulted in ACD or in a positive patch test, but also to discover new or rare skin sensitisers not (yet) found in commercial products or to identify new sources of already known contact allergens. In some patients – for example, children, having fewer exposures and only limited space on their backs – testing own products and their (potential) ingredients is sometimes prioritised as opposed to (large) standardised patch-test series. In addition, on occasion, other test methods than patch-testing are needed. We provide a brief and practical overview for clinicians on how to test selected own materials brought in by patients, based on the literature and on the authors' personal experience.

GENERAL CONSIDERATIONS

One should never patch test unlabelled products or items with an unclear composition; this applies particularly to occupational materials. Domestic products containing strong acids or alkali such as toilet cleaners, dishwasher tablets or oven detergents (eg those with a high sodium hydroxide (NaOH) content) should not be patch-tested. The same applies to cement, gasoline, (some) pesticides and, generally, highly toxic or poisonous chemicals. These should also not be patch-tested to avoid strong irritant, corrosive or (direct or systemic) adverse reactions. There are only rare exceptions in experienced patch-test clinics.[3] Besides, the risk of active sensitisation should always be kept in mind when testing own (occupational) products and dilutions in appropriate vehicles also need to be considered. When dealing with industrial chemicals or occupational materials containing complex chemical mixtures, it is strongly advised that the existing literature and reference works are consulted first, and/or cooperation is sought with chemists and/or pharmacists to evaluate the feasibility of patch-testing (if any). If no clear advice can be found on how exactly to patch-test a given product or chemical, it may be worthwhile to check the literature for the patch-test modalities of similar compounds for which (some) guidance may exist.[4] Modifications of the classic patch-test and/or additional investigations may need to be considered in selected cases (see Table I).

COSMETICS

Typical leave-on cosmetics (eg day and night creams, eye creams, body lotions and make-up items) can be applied 'as is' on a patch-test chamber. One exception to this is waterproof

TABLE I: MODIFICATIONS OF THE CLASSIC PATCH-TEST AND ADDITIONAL INVESTIGATIONS TO PATCH-TESTING[1,2,5,16,17,20]

MODIFICATION	DESCRIPTION
Semi-open test	The test consists of the application, by using a cotton swab, of a minute amount (ie a drop or ~0.05 mL) of a product on a skin surface of at least 1 cm^2. After evaporation, the test area is covered with an acrylic adhesive paper tape (eg 3M Micropore paper tape). The same reading criteria as for occlusive patch tests are used. The test is most often done with products that would easily irritate upon patch-testing (eg rinse-off cosmetics, waterproof mascara and nail lacquer).
Repeated open application test (ROAT)	This test consists of the application of a product (or a suspected ingredient) twice daily on the volar side of the forearm. This is applied for at least 10 days or until a papulo-vesicular or follicular reaction appears, sometimes with local spreading, covering at least 25% of the application area. ROAT is most often done for suspected leave-on cosmetics (that may patch-test false-negative!) or for suspected eye drops (that often patch-test negative). Rinse-off products (appropriately diluted!) and occupational products (contacted during work, with an acceptable pH (4–9) and a known chemical composition) can also be tested in this way.
Glove-repeated application test (GRAT)	The method consists of applying a piece of a suspected glove (3 × 3 cm), and alternative gloves, to the volar side of the lower arm. They are fixed with a non-adherent bandage for approximately 8 hours a day (ie overnight) for 10 consecutive days. GRAT might be more reliable than (only) patch-testing pieces of suspected gloves.
Patch-testing extracts of own products	The suspected material is placed in a container, completely submerged in a solvent (acetone, water or ethanol) and extracted for a certain time, usually by means of an ultrasonic bath, resulting in a liquid containing (concentrated) components. The filtered extract can then be patch-tested, often after further concentration by evaporating the solvent. Once completely evaporated, the residue is first redissolved in 0.5–1 mL of solvent before patch-testing. The ideal extraction solvent and extraction time are material-dependent and can sometimes be found in the literature. Testing with extracts appears to be more sensitive than testing materials 'as is' (eg in the case of gloves).
Dilution series	A dilution series of a product or an ingredient in a product may be used to differentiate a true allergic reaction from an irritant (false-positive) one: the product or individual chemical is 'serially diluted', usually in a liquid vehicle (eg 1%, 0.32%, 0.1%, 0.032%, 0.01%, 0.0032%, 0.001% and 0.00032%, with a tenfold difference between every second concentration). If the reaction is due to a contact allergy, a gradual decrease in reaction strength with every lower concentration will occur, whereas in the case of irritancy a 'positive' reaction vanishes abruptly when the concentration is lowered.
Scratch patch test	Scratch patch-testing consists of applying a regular patch test on a scratched skin surface. First use an alcohol swab to clean the patient's back approximately where the scratch patch test will be applied. Leave it to dry completely. Then use a 30-gauge needle to scarify the skin in a parallel straight diagonal pattern. The pressure needs to be sufficient to cleave the stratum corneum without creating blood punctures. Then apply the patch test, as is done in regular patch-testing. Possible applications are eye drops and other (systemic) drugs.
Strip patch test	Strip patch-testing consists of 10 or more repeated applications of adhesive tape (3M Transpore surgical tape) on the skin before placing the patch. A possible application is eye drops and other (systemic) drugs.
Booster patch test	When a patch results in a doubtful patch-test reaction (?+), performing a repeat patch test may be considered. Occasionally, if the dubious reaction is a very weak but a truly allergic one, then this may result in a more clearly positive patch-test result (+ or higher) by 'boosting' the immune response.

mascara: it should always be patch-tested semi-open to avoid irritant (even bullous) reactions. The following can be summarised for other types of cosmetics:[2]

Cleansing milks and make-up removers: are most often patch-tested 'as is' (especially if no rinsing is performed), although some authors prefer to test them semi-open[5] and/or diluted 20% (in an appropriate vehicle, usually petrolatum or water) in occlusive testing. The former test method is very practical as it can be performed immediately when the patient is at the clinic. It consists of the application, using a cotton swab, of a minute amount (ie a drop or ~0.05 mL) of the product on a skin surface of at least 1 cm^2. After evaporation, the test area is covered with an acrylic adhesive paper tape (eg 3M Micropore paper tape). The same reading criteria as for occlusive patch tests are used. It should be emphasised that some make-up removers, especially 'bi-phasic' ones, that is, with a water and oil phase, often contain irritant solvents such as isohexadecane, isododecane or isoparaffin. These solvents may easily provoke irritant reactions when patch-tested and, clinically, as irritant contact dermatitis (ICD) (eg on the eyelids).[6]

Deodorants, toilet waters (eaux de toilette) and perfumes: are usually applied 'as is' on a patch test.

Shampoos, bar soaps, bath/shower gels and shaving foams: are often tested semi-open. Patch-testing is an alternative, usually in a 1–10% dilution in aqua.

Hair conditioners, hair sprays and gels: can be tested semi-open or under occlusion in dilutions up to 20% (in an appropriate vehicle, usually petrolatum or water). Specific hair-care products such as silicone- and oil-based cosmetics may also be applied 'as is' to a patch. Hair dyes should be tested semi-open – both the colourant and the oxidiser, and also a 50 : 50 mixture of both. Permanent-wave solutions might need the pH to be adjusted

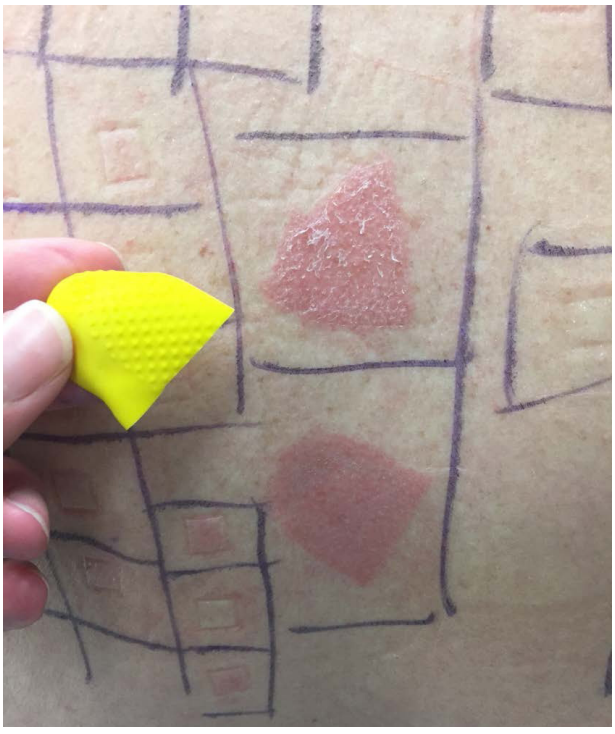

Figure 1: Strong positive patch-test reaction (++) to pieces of a glove fixed to adhesive tape (semi-open) on the back

before they are applied to the skin; they can be tested semi-open or occluded up to 5% in petrolatum.

Toothpastes: are generally tested semi-open and/or patch-tested diluted (5–50% in petrolatum). Many toothpastes seem to have become less abrasive than before, hence, patch-testing is often possible 'as is'– or can even be considered necessary, as dilutions or semi-open testing might miss contact allergy to them.[7]

Nail lacquers: the classic ones (nowadays often containing copolymers based on adipic acid/phthalic anhydride) can be tested semi-open or on patch after allowing sufficient evaporation. (Meth)acrylate-containing UV/LED-cured nail polishes are tested only semi-open. It is recommended that screening agents (eg hydroxyethyl methacrylate (HEMA) 2% in petrolatum) be tested first because simultaneous testing of several (meth)acrylate-containing gels often results in multiple (severe) positive reactions, which might give rise to an 'angry back' phenomenon.

Wet wipes: can be applied 'as is' (eg 5 cm^2) fixed on acrylic tape. Alternatively, the liquid of a wipe can be collected and patch-tested 'as is', although this may occasionally provoke some skin irritation.

NON-COSMETIC CONSUMER PRODUCTS

Household detergents (eg dishwashing liquids or all-purpose cleaners): are often not patch-tested in our clinic in contrast to their ingredients, such as fragrances and preservatives, which are present in commercial products. Nevertheless, if tested 'as is', a pH control is needed and, when the pH is acceptable (ie pH <9 and >4), semi-open testing can be performed. Alternatively, they can be patch-tested in dilutions such as those for rinse-off cosmetics (ie 1–10% in petrolatum).

Paints and glues: domestically used paints and glues, which often contact the skin when they are handled, can be tested semi-open.

Solid materials (eg gloves, textiles, leather, shoes, sanitary pads, spectacle frames, metal, plastic and rubber consumer items): pieces or scrapings of the product are usually patch-tested 'as is'. It is important, whenever feasible, to try to obtain sufficient material and/or to apply large enough pieces, because the culprit allergen(s) may be present in low concentrations and/or may not be homogeneously distributed throughout the material. Sometimes scrapings are placed in a small amount of petrolatum and patch-tested (eg spectacle frame scrapings[8]). For other less delicate materials, though, larger pieces (usually up to approximately 5 cm^2, eg, textiles, leather, gloves) – in triplicate, moistened with water, ethanol or acetone, respectively, are placed on the back or on the outer side of the upper arms, and fixed with adhesive tape (see Figure 1). In the case of metals or any other solid materials, it is important to be careful of sharp edges.

Sometimes different parts of a given item need to be tested: for example, the inside and outside of sanitary pads,[9] gloves.[10] The different components of diabetes devices, sometimes containing several possible sensitisers that 'migrate' from the inside to the skin-contacting outer layers of the material, may also have to be tested.[11]

Patch-testing with (much) smaller pieces is an alternative, but false-negative reactions can then occur more easily. In addition, it is advisable to have late readings (day 7 or sometimes even later) and/or to leave the pieces or scrapings occluded for 3–4 days instead of the usually recommended two days. The rationale for doing so is that low-concentrated allergens that are 'fixed' in the materials may take longer to leave them and penetrate the skin.[12] Such adaptations require additional control testing to exclude irritant or false-positive reactions.

Testing extracts is also possible: the material is then placed in a container, completely submersed in a solvent (acetone, water or ethanol) and then extracted for a certain time in an ultrasonic bath, resulting in a liquid containing (concentrated) components. The filtered extract can then be patch-tested, often after further concentration by evaporating the solvent (eg for gloves, textiles,[13] leather[14] or diabetes devices[15]). After complete evaporation, the residue is first redissolved in 0.5–1.0 mL of solvent before patch-testing.

The ideal extraction solvent and extraction time may differ depending on the material under investigation and, occasionally, some guidance can be found in the literature. Testing with extracts appears to be more sensitive than testing materials 'as is'.[16] Regarding ACD from gloves, a glove-repeated application test (GRAT), similar to the ROAT, has recently been proposed by French researchers; it may be more sensitive than (only) testing rubber contact allergens and pieces of gloves tested 'as is'.

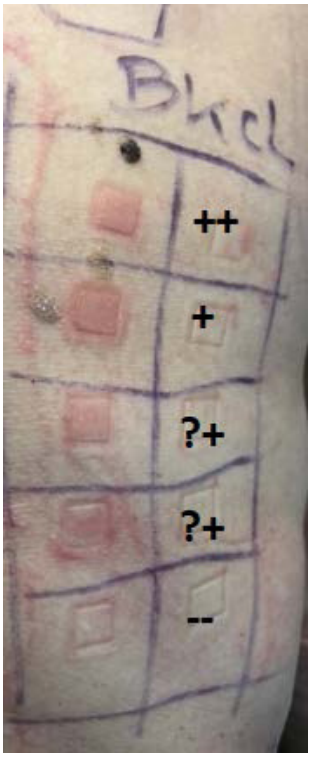

Figure 2: Gradually decreasing positive patch-test reactions to a dilution series (0.1%–0.005% in water) of benzalkonium chloride (BKCL), a notorious skin irritant but also a sensitiser. This pattern suggests contact allergy rather than irritancy.

The method consists of applying a piece of a suspected glove (3 × 3 cm), and possibly also alternative gloves, to the same site on the volar side of the lower arm, fixed with a non-adherent bandage, for approximately 8 hours a day (ie overnight) for 10 consecutive days.[17]

MEDICATION, ANTISEPTICS, DISINFECTANS AND FOOD ITEMS

Systemically administered drugs (eg tablets, intravenous solutions, cough syrups and food supplements): when a delayed-type allergic reaction from a systemically administered drug is suspected, both adults and children can be patch-tested with the suspected agents, even when the clinically adverse reaction involved a severe cutaneous adverse drug reaction (SCAR, eg drug reaction with eosinophilia and systemic symptoms (DRESS), acute generalised exanthematous pustulosis (AGEP) or toxic epidermal necrolysis/Stevens-Johnson Syndrome (TEN/SJS)).[18] Ideally, 4–6 weeks after resolution of the drug rash (and usually six months for DRESS), 10% of the active principal in petrolatum should be patch-tested. If not available, either an alternative patch-testing of the commercial tablets at 30% in petrolatum can be carried out or an attempt can be made to make a test preparation from the commercial drug so that the final preparation contains 10% of the active ingredient. In the case of SCARs, some authors prefer to start with higher dilutions (eg 1% instead of 10%). Apart from petrolatum, other vehicles (water, ethanol) may be considered, depending on the solubility of the drug.

As to the test site, a particular case concerns fixed drug eruptions (FDEs) for which the suspected drug needs to be patch-tested on residual (pigmented) skin locations of the drug eruption, that is, where the memory T-cells reside.[19] With FDE, a first reading on day 1 is often feasible. When obtaining a positive result, especially with a new drug, an adequate number of controls should be included. Patch tests with medication may be falsely negative and further skin testing (eg prick tests and/or intradermal tests, with late readings) should be considered case by case (eg with maculopapular eruptions, and even in some cases of SCARs such as DRESS. In the case of TEN/SJS, the intradermal test methods are not recommended and with FDEs they appear to be of less value (personal observation)).

Topical medicaments: can be patch-tested 'as is'. When irritant substances are present, such as benzoyl peroxide or tretinoin, then a ROAT and/or a dilution series may also be necessary (see below). For topical corticosteroid creams and ointments, and aminoglycoside-containing preparations, late readings (day 7) are important in order not to overlook contact allergy to them. Eye drops and gels often result in false-negative patch-test reactions, so it is useful also to consider scratch-patch or strip-patch tests[20] and to perform ROATs, or even use tests (ie re-using the suspected product under normal use conditions)".[21] Recent literature has stressed the potential value of scratch-patch testing not only with topical ophthalmic products, but also in cases of drug eruptions, including systemic allergic dermatitis (SAD) and even SCARs (eg AGEP or DRESS – personal observation).[22,23]

Antiseptics (eg ethanol- or isopropanol-based hand antiseptics): can usually be tested 'as is' if they are used as a 'leave-on' product. If rinsing is needed, then a semi-open test is advised. Disinfectants used for surfaces and equipment require a pH control. If the pH is acceptable and skin contact 'as is' effectively concurs, a semi-open test or patch-testing 1–10% in water or petrolatum may be advised.

Food items: in addition to ACD, they may also produce contact urticaria and/or protein contact dermatitis (PCD), for which prick or scratch-patch testing with immediate readings is requested. As PCD concerns a mixed mechanism (Type I and IV), patch testing may occasionally also result in a delayed reaction (eg to mango).[24]

OCCUPATIONAL PRODUCTS

Nearly one-fifth of occupational ACD can be diagnosed only by testing with the products handled at the workplace.[10] Nevertheless, patch-testing them can be difficult, as it is often not easy to ascertain exactly which components they contain. Therefore, it is important first to consult the (material) safety data sheets ((M)SDS) in which components indicated with H315 ('can cause skin irritation') or especially H317 ('can cause an allergic reaction') are most relevant.[25] It is also useful to check for the synonyms of components mentioned in the (M)SDS or on the product labels and to search the so-called chemical abstracts service (CAS) number of a chemical substance (ie a unique numerical identifier, regardless of any synonyms) or consult databases (eg https://pubchem.ncbi.nlm.nih.gov/). Recently, a patient was observed at our Antwerp Contact Allergy Unit who had developed an airborne ACD from triethanolamine contained in a foam insulation spray. This was indicated in the SDS as 2,2',2''-nitrilotriethanol (personal observation). Unfortunately, the

data in SDS sheets are rarely complete (eg failure to mention the presence of methacrylates in anaerobic glues).[2,25]

An occupational product can often be tested 'as is' semi-open if the patient possibly has direct skin contact with it (eg glue or paint). With patch-testing, dilutions in appropriate vehicles should be made according to the literature[1,2] or following de Groot's recommendations.[26] Attention should be paid to the fact that (the sum of) some components in the final test preparation obtained should not be present in concentrations above their recommended test concentrations (eg acrylates maximum 0.1%; methacrylates maximum 2%).[2] When the product is water-based, it is important always to check the pH (acceptable in a range between 4 and 9).[1,2] In some clinics, buffers are used to adjust the pH, if necessary. Merely diluting the product does not correct the pH, as very high dilutions would be required to adjust the pH, causing potential sensitisers to be over-diluted. When testing (potentially irritant) occupational products for which not much guidance exists, application on the upper arm (rather than the back) may be advised, with a first reading on day 1 instead of day 2.[10]

In addition, a serial dilution series can be used, as is generally done for new allergens and for some chemicals that possess both irritant and sensitising properties, such as benzalkonium chloride (personal observation) (see Figure 2) and didecyl dimethyl ammoniumchloride[27] (see below).

Unused (undiluted) water-based metalworking fluids (MWFs) should be diluted and tested 5% in water, whereas oil-based products can be tested 50% in olive oil. It is important also to test the 'used' MWFs, as distributed throughout the machine, as these may contain several additives (eg metals, biocides, fragrances and derivatives of 'tall oil' – rosin or colophonium) that are not necessarily present in the unused materials.[1,2] We habitually test used (diluted) MWFs from the workplace first in a semi-open test, as they come into contact with the skin. If water-based, then the pH is checked first and possibly adjusted (range 4–9). If semi-open testing remains (false) negative, the products are tested under occlusion.

Powder or dust from the workplace can sometimes be patch-tested in a chamber moistened with water,[28] although false-negative reactions should be kept in mind.[4]

Epoxy resin systems, isocyanates (polyurethane) and acrylates brought from the workplace, should be diluted according to the recommendations[2,26] in case patch-testing with the baseline series remains inconclusive. Note that commercial isocyanates are notoriously false-negative when patch-tested.[29]

In addition to contact allergy, other factors such as wet work, chemical irritation and/or mechanical strain must also be considered, all of which are relevant to occupational dermatitis.[30]

PLANTS AND WOODS

Different parts of plants (flower, stem, leaf, root) should be patch-tested semi-open, but caution is advised as some plants may provoke strong irritant and/or toxic skin effects, or even active sensitisation.[1,2] It is advisable to consult informative databases (eg https://www.botanical-dermatology-database.info) and to consult colleagues who have more experience in testing plants. In addition, take a good history to find out exactly how patients come into contact with plants and plant-related products, the latter sometimes being the actual cause of the problem (eg flower food).[31] Tropical woods can be tested either semi-open or patch-tested up to 10% in petrolatum; however, strong positive allergic and, in part, irritant reactions can still occur.[32]

HOW TO HANDLE REACTIONS TO OWN PRODUCTS

Here we offer suggestions for handling reactions to own products using, first, a positive patch test, then a negative patch test and, finally, a doubtful patch test.

A POSITIVE PATCH TEST

A positive patch test to an own product 'as is' may present a potential 'false-positive' reaction and therefore control tests in unexposed (healthy) individuals should also be performed to exclude such reactions. In addition, a dilution series may be used to differentiate a true allergic reaction from an irritant (false-positive) one: the product (or individual chemical) is serially diluted, usually in a liquid vehicle (eg 1%, 0.32%, 0.1%, 0.032%, 0.01%, 0.0032%, 0.001% and 0.00032%, with a tenfold difference between every second concentration). If a reaction is due to a contact allergy, a gradual decrease in reaction strength with every lower concentration will occur, whereas in the case of irritancy a 'positive' reaction vanishes abruptly when the concentration is reduced (see Figure 2).

When a mixture or product results in an allergic-positive skin reaction, continued testing with individual ingredients, if feasible and/or available (eg cosmetics, pharmaceuticals), should be done to identify the actual culprit(s). Many cosmetic companies nowadays provide the individual ingredients at adequate concentrations and vehicles for patch-testing ('patch-test kit'). However, an ingredient concentration diluted down to the concentration as used in the finished product may be too low and lead to a false-negative reaction, even at a day 7 reading.

The optimal (reliable) patch-test concentration of a given substance can be up to 10× or 20× its use concentration in the corresponding finished product.[33] Repeated testing in a higher concentration and/or a more appropriate vehicle may then be appropriate. Although time-consuming, ROATs with individual (low-concentration) ingredients may also be considered. A ROAT is performed twice daily for up to 10 days, or until a papulovesicular or follicular reaction appears, sometimes with local spreading and covering at least 25% of the application area[34] (see Figure 3). But caution is advised, because not everything can be tested with a ROAT: only leave-on products, appropriately diluted rinse-off products and occupational products effectively contacted during work, with an acceptable pH (4–9) and a known chemical composition, can be tested. Sometimes the synergistic effect of individual components in a 'mixture' (ie a finished cosmetic product) may facilitate skin penetration of an individual ingredient and therefore occasionally act as a better vehicle for the sensitising culprit, as opposed to plain water or petrolatum. Many examples of this synergistic effect have been cited in the literature: for example, topical pharmaceutical products and medical devices containing sorbic acid or potassium sorbate.[35]

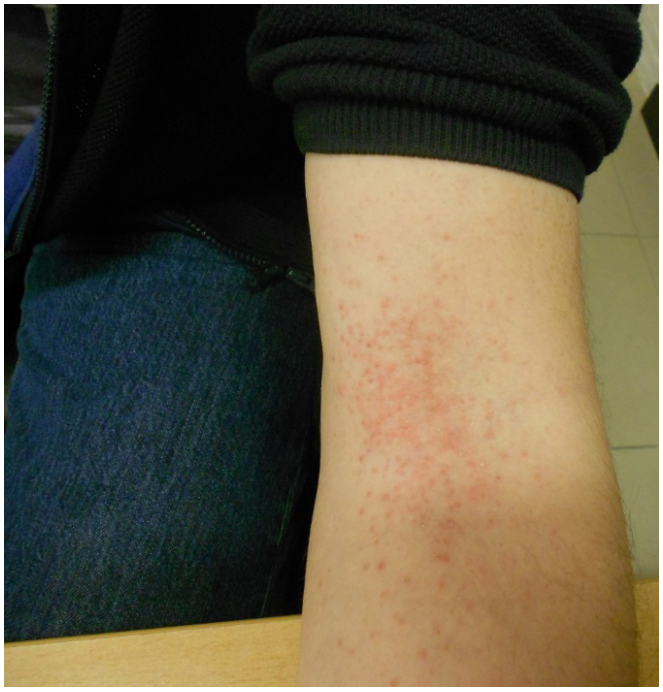

Figure 3: Positive repeated open-application test (ROAT) to a lip balm suspected to have caused cheilitis. Note the follicular reaction and the local spreading compatible with a contact allergic response.

Another explanation, although one that occurs more rarely, is a so-called 'compound' allergy, that is, the occurrence of contact allergy to a newly developed substance in a mixture. Cosmetic and other products, in addition to their individual ingredients, may contain additives or impurities as hidden sensitisers (eg formaldehyde, isothiazolinones, benzophenones, fatty alcohols, dimethylaminopropylamine).[36–40] In the case of cosmetics, it may be worth checking their technical dossier and full composition, possibly including additives and degradation products (Personal communication Ewa Daniél; Sensitising additives and impurities in raw materials, European Society of Contact Dermatitis congress, 8–10 June 2022, Amsterdam, The Netherlands).

A NEGATIVE PATCH TEST

A negative patch test to a (highly suspected) own product 'as is': this may possibly present a false-negative reaction, that is, the culprit ingredient(s) might be present in too low a concentration to provoke a reaction to single occlusive patch-testing.[41] If allergy is strongly suspected, the patch test can be repeated ('boosting'), and/or a repeated open application test (ROAT) can be performed with the product 'as is' (eg cosmetics/pharmaceuticals). When positive, patch tests with the individual ingredients and in appropriate concentrations and vehicles should be performed. Rarely, ROATs with a product tested 'as is' may not induce a reaction on the ROAT location but rather at a distance, that is, at the initially involved skin location.[42] Finally, ROATs do not always distinguish reliably between allergy and irritancy, the former sometimes characterised by a follicular and/or a spreading reaction (see Figure 3).

A DOUBTFUL REACTION

A doubtful reaction to an own product tested 'as is' – as in the case of individual chemicals – can be difficult to interpret since it may concern an irritant, but also a positive allergic (yet very weak) reaction. A ROAT or a re-testing of the product, usually at a different skin location, may be considered ('boosting' of the response) in such instances.

CONFLICT OF INTEREST

Olivier Aerts is an investigator, consultant and/or speaker for Leo Pharma, Abbvie, L'Oréal/La Roche Posay and Bioderma/NAOS. The other authors have no conflicts to declare.

This article has been peer-reviewed.

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