Art and science of patch testing

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The diagnosis of a contact allergy represents several important and essential steps since the failure to recognize a contact allergy can occur in any of the various stages of the contact allergy investigation. Besides patch testing, which is the gold standard to identify contact allergens, other skin-testing methods may be required. However, their application requires motivation and industry on the part of the investigating physician.

It is evident that the more experienced the investigator, the more accurate will be identification of allergens. Moreover, his/her knowledge must be on the basis of good training, updated with the literature, attending courses, CME programs and websites (with respect to this, we offer information via internet on our website www.cdeskpro.be,), etc. One must be eager to detect the allergen(s), i.e. like "Sherlock Holmes like" approach should be adopted.[1]

DETECTION OF THE ALLERGEN(S)

To make a correct diagnosis and to identify the allergen(s), one should have the basic knowledge regarding the chemicals contacted, a detailed history of the patients, information regarding the several forms of exposure. Also the clinical symptoms and the localization of the lesions should be examined carefully. Of course, patch testing at present remains as the only reliable test to identify a contact allergen. It should be performed as extensively as possible in order to cover all the potential allergens that are in contact with a particular subject. Besides patch testing, other types of skin tests such as open and semi-open tests, repeated open application tests (ROAT), usage tests and even prick tests (in order to detect a protein contact dermatitis) may be required. The most important step, however, is the determination of the relevance of the positive skin reaction observed, for which the potential cross reactions also should be considered.

SKIN TESTS[2]

One has to realize that only an allergen that is tested can be detected. However, one should never test completely unknown products.

1) Patch tests

The patch test is a biological test; hence, the results can be erroneously negative or positive. Sometimes concentrations, vehicles and reading times (later than 4 days) should be adapted (as is the case with corticosteroids, for example). Patch testing with a standard series is essential; however, the tests with additional series and the products supplied by the patient along with their ingredients are equally important.

At times, it happens that the cited allergen is not itself the cause of the allergic reaction but an impurity present in it. Moreover, allergenic degradation products may be formed during storage, for example, by oxidation as is the case for limonene.

When testing the products such as solid materials, e.g. shoes, textiles, paper and plants or when insufficient amounts of allergen are released, extracts may have to be prepared.

The allergens, usually incorporated in petrolatum (at times a different vehicle can be used), are applied in round or square chambers, which are mounted on an adhesive tape, on the upper back of the patients for a period of 2 days. The readings of the test results are obtained approximately 20 min after the removal of the patches and again after 3 and/or preferably

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4 days (at times even later). Erythema, edema, papules, sometimes accompanied by small vesicles extending slightly beyond the patch test border indicate contact allergy. At times, dilution series are used to detect the sensitivity level of the patient and to determine the relevance with regard to the actual-use situation.

2. Photo-patch tests

In case of photo-allergic reactions, photo-patch tests must be performed: the allergens are tested in duplicate on the back and irradiated with UV light (most often UV-A 5 J/cm^2). Readings should be immediately recorded post-irradiation and 2 days post-irradiation. Further readings at 3 and 4 days post-irradiation are desirable to enable the detection of crescendo or decrescendo scoring patterns suggesting allergic and nonallergic mechanisms, respectively.

3. Open and semi-open (or semi-occlusive) tests

These tests are useful modifications for the products that have an irritation potential.

With an open test, the substance is applied uncovered on the upper arm or upper back twice a day for a period of at least 2 days without washing the test site.

The semi-open test comprises the direct application of a minute amount (1 to 2 μl) of a liquid with a cotton-tip applicator on the skin surface in an area of approximately 1 cm^2 [Figure 1]. After the complete evaporation of the liquid (the excess can be removed with a filter paper or another cotton-tip applicator, the test site is covered with an acrylic tape. Water-soluble products can be tested as 1-2% aqueous solutions in this way. The reading of the skin test is performed at 2 and 4 days (at times later) as with regular patch testing.

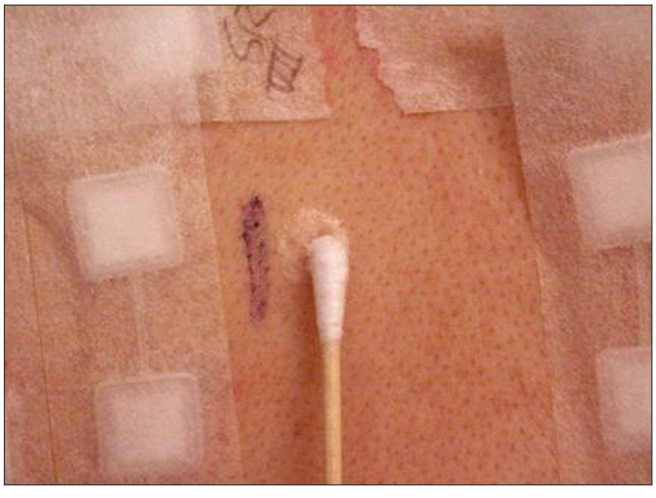

Figure 1: Semi-open test

With regard to the conditions of use, this test method is not based on scientific research but on longstanding expertise. The performance of the semi-open test depends mainly on the nature of the products the patient brings with himself/herself. The purposes of such testing are as follows:

- A practical and rapid method in case multiple products brought in by the patients must be tested.
- To avoid false-positive or irritant reactions by patch testing potentially irritating products. However, this does not imply that a semi-open test cannot give rise to an irritant response. Corrosive products and products with a pH < 3 or > 11 should never be tested. In the latter case, buffered products can be tested.[3] One may test the potential allergenic ingredients individually.
- To avoid false-negative reactions by testing extremely diluted products, for example, in case of a contact allergy to a fragrance ingredient or a preservative in a shampoo. However, in case of a negative semi-open test, the possibility of a contact allergy might not be excluded completely. It is indeed possible that the allergen is present in an extremely low concentration so as to produce a false negative test. This also points to the importance of testing all the ingredients separately in an appropriate concentration and vehicle in case a contact allergy is really suspected.

Practical applications

Numerous products with a mild allergenic potential can be tested using the semi-open test method, provided that the results are interpreted carefully and confirmed by testing with diluted products and certainly with the individual ingredients. The products include the following:

- Pharmaceutical products: Products that could produce irritant reactions under patch-test occlusion, for example, products containing antiseptic agents such as mercurial compounds (e.g., phenylmercuriborate), quaternary ammonium salts such as benzalkonium chloride and iodine, antiseptics containing emulsifiers such as lauraminoxyde (Hibiscrub®) and nonoxynol (e.g., (Iso)betadine®, Hibitane®, Hexomedine transcutanée®); products containing solvents such as propylene glycol in high concentrations; creams based on the emulsifier sodium laurylsulfate.
- Cosmetic products: Products containing emulsifiers, solvents or other substances with an irritant potential such as mascara, nail lacquers, hair dyes, shampoos, permanent-wave solutions, liquid soaps and peelings.
- Household and industrial products: After having verified whether the pH is not too low or too high or that a

corrosive material is not involved, the semi-open test can be useful for a number of products such as paints, resins, varnish, glue, ink, wax and soluble oils.

4. Use tests and/or ROATs

Patch tests are vastly different from normal use conditions; therefore, the tests can be completed by the provocative use testing of sensitized subjects. In fact, when dermatitis occurs after repeated exposure or after the use of products such as cosmetics on sensitive skin areas such as the face and a negative patch-test result is obtained, use tests and/or "repeated open application tests" (ROATs) are recommended. The intention is to approximate the use situation as nearly as possible.

With ROATs, approximately 0.1 ml of the test material is applied twice daily to the flexor aspect of the forearm near the cubital fossa, to an area of approximately 5 × 5 cm. The results are interpreted after 1 week; however, at times, ROATs must be performed up to 21 days, particularly with low-concentrated allergens to reveal an allergic reaction.

The contact-allergic reaction often starts as a follicular reaction.

DETERMINATION OF RELEVANCE

The allergy examination reaches a crucial phase when a positive reaction is found, for which the relevance of that reaction must be determined. One may not conclude too quickly that a test reaction is not relevant because such a determination depends primarily on the expertise of the investigator and the possibility of detecting the allergen in the environment of the patient. Occasionally, the chemical relationship between the molecules will help to understand the cross-reactivity patterns. Hence, an allergen might be found that itself is not relevant with respect to the dermatitis of the patient but which cross-reacts with the actual culprit. This is the case, for example, for paraphenylenediamine that cross-reacts with chemically-related diaminodiphenylmethane, a marker to detect contact allergy to isocyanate or polyurethane resins.[4]

In certain cases, it might be interesting to perform chemical analysis[5] not only to confirm the presence of a certain allergen in the contacted materials, thereby determining the relevance, but also for the identification of the allergens.

ADVICE TO THE CONTACT-ALLERGIC PATIENT

Once an allergen has been identified, it is the dermatologist's task to provide specific advice regarding the products that have to be avoided or regarding the products that can safely be used since subjects sensitive to specific ingredients must avoid the products containing them. Our PC program available on the website www.cdeskpro.be is a help desk by the Contact Allergy Foundation; this help desk aims to increase the knowledge and distribute the information on contact allergy more widely to the medical profession and patients, pharmaceutical and cosmetic (or other) industries as well as to the government and research centres concerned. It also contains information on topical pharmaceutical and cosmetic products along with their complete composition. Patients allergic to such ingredients get a list of topical pharmaceutical products that contain the allergen(s), which helps in its avoidance. Moreover, although cosmetic labeling exists, in our experience, providing the allergic patient with a limited list of cosmetics that can be used is the most practical and effective method.[6]

CONCLUSION

If the results of the skin tests are negative for a patient for whom the diagnosis of allergic contact dermatitis has been proposed, one has to go back to the beginning, that is, with a thoroughgoing anamnesis (perhaps with a visit to his or her environment). The assumed allergens must be retested (perhaps in another concentration, with another vehicle or with another testing method) and the additional allergens must be tested. The patient can also be asked to maintain a diary in the hope that some correlation can be discerned between the exposure to a substance and the occurrence of the skin problems.

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