

New aspects in allergic contact dermatitis

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Purpose of review

To give selected new information on contact allergy and allergic contact dermatitis with focus on diagnostic procedures and pitfalls.

Recent findings

Recent studies dealing with common contact allergens have improved our understanding of the relationship between positive patch tests and the clinical interpretation and consequences for the patient.

Summary

Nickel allergy is still the most common contact allergy in Europe in spite of full implementation of the EU Nickel Directive in 2001. Contact allergens in cosmetics and topical drugs are another common cause of allergic contact dermatitis. The main culprits include fragrance chemicals, preservatives, and hair dyes. We are all more or less exposed to cosmetics and topical drugs on a daily basis. The labelling requirements given in the Cosmetics Directive is of great help in tracing the causative allergenic ingredients. Most of the components present in cosmetic products are also occurring in household and industrial products, often under other trade names. Patients with multiple contact allergies constitute a special problem because their quality of life is severely affected by the multitude of eliciting products in the environment. We still lack a good understanding of why these patients become so easily sensitized.

Keywords

compositae dermatitis, contact allergy, contact dermatitis, cosmetics, nickel, patch tests, topical drugs

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Introduction

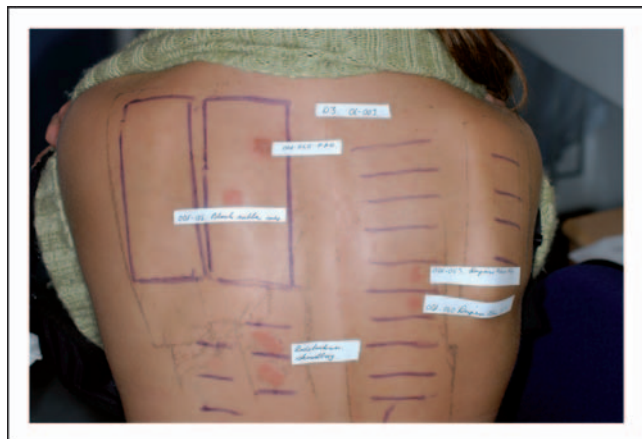
Contact dermatitis is a field under constant development because the environment changes over time due to introduction of new chemicals in consumer and industrial products and phasing-out of other chemicals. Fortunately, the diagnostic procedures are also under constant refinement together with improved understanding of pathogenic mechanisms behind contact allergy and allergic contact dermatitis. This review gives selected new information.

Diagnosis of contact dermatitis

Contact dermatitis is a multifactorial disease and, apart from exposure to sensitizers and irritants, many individual and environmental factors influence the development of the disease. These factors include preexisting skin disease as atopic dermatitis, regional variation in skin susceptibility to develop contact dermatitis, mode and duration of exposure. All types of eczema may be caused by, or complicated by, contact allergy. You cannot by clinical evaluation decide whether eczema is allergic or nonallergic in nature.

The diagnosis of irritant contact dermatitis is based on known exposure to irritants, wet work, frequent use of gloves and hand washing and exclusion of allergic contact dermatitis by patch testing with a minimum baseline series supplemented with selected products and allergens based on exposure history and review of ingredient lists and data sheets.

When establishing the diagnosis of allergic contact dermatitis, two criteria should be fulfilled: demonstration of contact allergy by a positive patch test with a nonirritant concentration of a contact allergen and demonstration of clinical relevance of the positive test by exposure history in combination with the dermatitis pattern. Although establishing clinical relevance may be easy in many patients, it may also require lengthy questioning of the patient to obtain the necessary clues to make a well founded conclusion (Fig. 1). To increase the accuracy of the evaluation of the relevance of a positive patch test, additional procedures may be useful, such as retests and serial dilution patch tests with the allergens in question, repeated open application test (ROAT) or use test [1]. In the case of a product brought in by the patient, chemical

Figure 1 The patch test procedure is easy

The challenge is selection of allergens to be tested, reading and interpretation of the reactions.

analysis and information collected from the manufacturer may be warranted.

Epicutaneous sensitization versus allergic contact dermatitis

Among individuals exposed to contact allergens, only a fraction get sensitized, and among these some will develop clinically manifest allergic contact dermatitis. The contact allergy may be lifelong, but the dermatitis often heals when exposure to the allergen is avoided. Some allergens are easy to avoid, whereas others are ubiquitous in modern life environment. Most epidemiological studies on contact dermatitis focus on contact allergy that is sensitization documented by a positive patch test and not allergic contact dermatitis. Evaluating the relevance of a positive reaction is one of the most difficult parts of the patch test procedure and depends on the dermatologist's interest and experience.

The prevalence of contact allergy among adults in the general population is around 20% [2,3^{*}], and among children and adolescents, the prevalence is nearly the same [4,5]. The lifetime prevalence of allergic contact dermatitis is more difficult to estimate, and prospective studies in unselected populations are missing.

Common contact allergens

Nickel

Nickel is still the most common contact allergen in the European Union in spite of the EU Nickel Directive, which was fully implemented in 2001 [6]. The incidence of nickel allergy in Denmark is decreasing in the younger age group, probably due to the fact that the nickel regulation was implemented in Denmark in 1992 [7]. The most common cause of sensitisation was ear-piercing. The continued high level of nickel sensitivity may be explained by

several factors, inter alia, occupational nickel exposure, exposure to nickel releasing items not covered by the directive, and personal import of nickel-releasing products from countries without a nickel regulation. An interesting finding among school children is that the application of dental braces before ear-piercing reduced the risk of nickel allergy compared to those children who had their ears pierced before the application of dental braces [8]. Many orthodontic appliances contain nickel and their clinical relevance in nickel-allergic patients has been discussed. A new study concludes that adverse reactions to orthodontic appliances has been observed, but are uncommon [9].

Cosmetic products: fragrances and preservatives

Cosmetic products are among the major causes of contact allergies and allergic contact dermatitis. Fragrances and preservatives are the main culprits. The European Cosmetics Directive (76/768/EEC) was implemented in 1976 with the main objective to safeguard public health, stating that cosmetic products must not cause harm to human health when used under normal and foreseeable conditions. However, the exposure to cosmetics is massive and it is inevitable that adverse effects occur, and allergic contact dermatitis from cosmetics is quite common. The Cosmetics Directive is regularly updated and the introduction of mandatory ingredient labelling is a major advantage for consumers and dermatologists in order to trace the allergenic compounds. The more recent introduction of mandatory labelling of 26 fragrance ingredients in cosmetic products, if their concentrations in the product exceed either 0.001% in leave-on products or 0.01% in rinse-off products, is a further improvement because fragrance allergy is an increasing problem. Now, household products must also be labelled for content of the 26 fragrance chemicals if present in a concentration of more than 0.01%. This new labelling requirement will enable fragrance-sensitized individuals to avoid contact with the relevant contact allergens. In routine diagnostic patch testing, fragrance contact allergy is screened using the fragrance mix (contains eight fragrance allergens). A new fragrance mix II (contains six fragrance allergens) has been developed to supplement the traditional fragrance mix. A multicenter study has shown that the new fragrance mix detected about 30% more fragrance allergic patients, who were missed by the old fragrance mix [10]. The fragrance industry has responded to the change in regulations by changing the composition of perfumes to reduce the occurrence of fragrance allergy. However, so far no effect on the frequency of fragrance allergy in eczema patients is documented. The European baseline patch test series has recently been amended to include fragrance mix II containing the six allergens: hydroxyisohexyl 3-cyclohexene carboxaldehyde (Lyrall), citral, farnesol, coumarin, citronellol, and α -hexyl cinnamal. Lyrall is the most important new fragrance allergen and is included as a separate patch test material [11^{**}].

Among preservatives, contact allergy to methylidibromoglutaronitrile (MDBGN) has increased from 0.7% in 1991 to 3.5% in 2000 [12]. MDBGN is widely used in household, industrial products, and cosmetics in particular. A change in the Cosmetics Directive was made in 2005 banning the use of MDBGN in stay-on products, and later also in rinse-off products. The effect of this regulation is already evident [13[•]], and this is a prime example of primary prevention. Clinical experimental studies in MDBGN-sensitive volunteer patients have documented the importance of repeated short-term exposures, as frequent hand washing with MDBGN-containing liquid soap could be a significant cause of sensitization and elicitation of allergic contact dermatitis to this preservative [14]. Further, reduction of the concentration in the product did not reduce the elicitation capacity if the number of exposures increased equivalently [15].

Hair dyes

Another major cosmetic allergy is hair dye allergy. It seems to be more common than previously reported [16]. The acute allergic contact dermatitis may be severe with scalp and facial oedema, which spreads to ears, neck, and shoulders. The patients are often misdiagnosed as angioedema and the patients are wrongly treated with systemic antihistamines instead of topical or systemic corticosteroids. Paraphenylenediamine (PPD) is the main indicator for hair dye allergy in the European baseline series. However, many of the other hair dye ingredients can sensitize. Most reactions are related to home-treatment and related to the oxidative (permanent) hair dye. A relationship between temporary tattoos, so-called black henna tattoos, and hair dye sensitization has been shown. The black henna is popular, especially among youngsters. It contains PPD in high concentrations and the tattoos carry a pronounced risk of causing primary sensitization. If the person then later dyes hair, a severe, acute oozing dermatitis in the scalp and face can develop.

Compositae

Compositae dermatitis in the classical clinical presentation is airborne pattern eczema. The hypothesis of airborne Compositae allergens has been difficult to prove. However, a recent Danish study has shown that feverfew-allergic patients are sensitive to airborne particles released from feverfew plants, and isolation of parthenolide in allergenic amounts from the particle-containing filters from the high-volume sampler is strong evidence of parthenolide as the responsible allergen [17]. The Compositae family of plants also comprises several medicinal plants that are used widely in modern herbal cosmetic (chamomile, arnica, marigold). It has been shown that compositae-allergic patients should be warned against topical use of Compositae-containing herbal creams and oils, not only because of the plant allergens, but also because of other allergenic cream constituents that cause

reactions in the group of patients who have multiple contact allergies beside Compositae allergy [18^{••}].

Corticosteroids

Allergic contact dermatitis to corticosteroids is an uncommon side-effect of topical therapy. It should be suspected in patients with long-standing dermatitis who do not improve during treatment with a topical corticosteroid, but it can also be seen as an acute dermatitis. Most common is reactivity to budesonide and hydrocortisone-17-butyrate. Recently, two groups have described a pustular eruption as a result of allergy to a topical corticosteroid. The eruption was classified as acute generalized exanthematous pustulosis (AGEP) like, although the patients did not have fever [19,20].

Rare contact allergens

Allergic contact dermatitis diagnosis presupposes that a dermatologist selects the correct allergens for testing a patient. If the relevant extra allergens are not tested, the diagnosis is missed. Therefore, patch testing with patient's own cosmetics, topical drugs and selected working materials is very important. Information from product data sheets, websites and textbooks are necessary tools in the procedure [21].

Among rare allergens are emulsifiers and surfactants that are widely used in cosmetics and topical products. They are also used as cleansing agents, and they are, by their nature, mild irritants. Due to their irritant properties, establishing of optimal patch test concentration is crucial. At least 25 consecutive eczema patients should be tested as controls with negative results in order to confirm allergic test reactions in the case patients. Recent case reports include two cases of decyl glucoside allergy from a hair mousse and the sunscreen agent Tinosorb M [22,23]. Emulsifier allergy may cause severe acute allergic reactions in some cases like oleyl alcohol in Elidel cream and sodium dihydroxycetyl phosphate in herbal cream [24,25].

Topical applications of skin care products containing antioxidants have become increasingly popular. Two groups [26[•],27] have described allergic contact dermatitis to hydroxydecyl ubiquinone (Idebenone), a synthetic analogue of Coenzyme Q-10 used in antiaging topical products. When dealing with new contact allergens, it is helpful to obtain the individual ingredients from the product manufacturer, and today many companies are willing to supply patch test material to dermatologists on request. The Crocs footwear was first introduced in 2002 and is now used in both children and adults. A case of allergic contact dermatitis to Crocs has recently been published and this case points to the potential difficulty in identifying allergens when a company is not willing to

provide information and manufacturing ingredients [28]. Chemical analysis may be needed to clarify the case.

Multiple allergies

Patients with three or more contact allergies may be defined as patients with multiple contact allergies [29]. In selected patients with suspected contact dermatitis, one out of every six to seven patients sensitized has multiple allergies, and in the general population, one out of every 21 patients has multiple allergies. The understanding of why some patients develop multiple contact allergies is limited and mainly based on assumptions. It seems that for the subgroup of multiple-allergic patients without high-risk exposure, it may be an inherent ability rather than a result of multiple exposures. Besides high-risk leg ulcer patients, it is not possible to identify patients at risk of developing multiple contact allergies. Patients with multiple contact allergies are typically elderly women who might have long-lasting and hard-to-treat eczema, and cumulative environmental exposure seems necessarily to develop multiple allergies [30•]. Cross-reactions as mechanism only explain a minor part of all patients with multiple contact allergies. Further studies on the subject could be of great interest.

Conclusion

Contact dermatitis is exciting and dynamic because we are all more or less exposed to allergens and irritants at home and at work. There are more than 3500 reported environmental contact allergens [31], and about 100 commonly causing allergic contact dermatitis. The majority rarely the culprit – but for the individual patient, the correct diagnosis and proof of contact allergy may be decisive for treatment, information and prevention. The interested dermatologist is encouraged to follow the development within this area by reading dermatology journals publishing papers on contact dermatitis.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 494–495).

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