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The Future of Allergic Contact Dermatitis as it Pertains to Cosmetics and Personal Care*

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Allergic contact dermatitis (ACD) describes a delayed type of hypersensitivity reaction that occurs when the skin comes into contact with a chemical to which it has previously been sensitized. A major development in ACD diagnosis was the creation of the patch test, which is credited to Josef Jadassohn[1] and was first described as a method to understand mercury-induced eczematous dermatitis in a syphilis patient. Patch testing involves applying patches containing various allergens on the upper back of an individual, removing the patches, then interpreting the skin's reaction to the allergens. While it is a brilliant technique, interpretation of the test results is yet to be perfected. Following are some aspects of this technique that require consideration, including the ingredients used, related legislative measures and testing limitations.

Clinical Relevance of Positive Patch Testing

Patch tests may signify an immunologic response but this response may have little or no clinical significance.[2–4] Currently, when a patch test is positive, the patient's history is further examined to aid in distinguishing whether this response is allergic or irritant in nature. The researchers then must ascertain whether the appropriate irritant controls are available, whether the morphology is that of ACD, whether the patient was previously exposed to the chemical, and a clinical course of action for once the chemical is removed.[5] Furthermore, if the patient is exposed again to the putative allergen without being patch-tested, such as via a provocative use test, it must be determined if the reaction will be reproduced.

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Clinical relevance algorithms have been offered by Marrakchi, Lachapelle, Ale and Hostynek to determine if another exposure will reproduce the allergic/irritant response.[2–5] Enhancing the quantitative understanding of clinical relevance would allow mathematical evaluations to determine the probability of a true clinical allergy given a positive patch test result. Probability mathematics would also add credibility to diagnoses. In addition, a uniform approach with the appropriate follow-up in a large series of patients could pave the way for probability theory and databases to determine the likelihood of patch test-related clinical relevance. As many chemicals in standard and special allergen series are found in cosmetics and personal care products, it is important to be certain that an individual is indeed allergic to a chemical before advising them to avoid products containing that chemical.

Improving Patch Testing

To further refine Jadassohn's patch testing, the following aspects could be addressed. These are important to the industry as many ingredients in cosmetic and personal care products have been documented to cause ACD, with some being more immunogenic than others.

Identifying the allergen: It is often assumed that a positive patch-test reaction clearly indicates the chemical causing it. For instance, when patch-testing with paraphenylenediamine (PPD) yields a positive result, it is assumed the patient is allergic to PPD. However one should also consider whether the patient could instead be allergic to a metabolite or degradant produced on the skin after contact with PPD.[7]

Even when an allergen is identified, as in the case of PPD in hair dye, there is still uncertainty as to how the body processes it and the critical immunogenic steps involved.[8] Furthermore, in the case of hair dye, allergens other than PPD may be overlooked. Therefore, knowledge of allergen structure, processing and recognition by the body may allow structural modifications of common allergens to allow their use without inducing allergic reactions.

In relation, natural products present a chemical identification problem because they can contain numerous allergens; thus, testing is nonspecific at best. This principle, illustrated by Hjorth's work on balsam of Peru,[9] deserves follow-up in regard to other complex chemicals. Lanolins also represent such a challenge. Overall, a clearer view of the chemical mechanisms of allergens and whether the true culprit is the allergen itself, a cross-contaminant or a skin metabolite

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is required. A better defined chemical structure as it relates to the clinical appearance of dermatitis would also allow for quantifying relationships with chemicals in commerce.[8]

TRUE-type test: Relatively little patch testing is performed in the United States, compared with Europe. Standardizing more allergens for US Food and Drug Administration approval is cost-prohibitive, which has led to a lack of investment. American dermatologists often use the Thin-layer Rapid Use Epicutaneous (TRUE) test[a] for the simplicity of its application,[6, 10] but a more efficient and convenient patch test with pre-dosed and standardized allergens is necessary. It must be commercially viable and easily applied to the patient without technical assistance. Involvement of the cosmetic and personal care industry is welcome.

Commercial availability and improvement of serial dilutions: Most patients are evaluated using the same patch test concentration[11] but not everyone reacts to the same concentration of a substance; some may react only to higher concentrations, thus allowing some exposure without phenotypic signs and symptoms. One fragrance mix, for instance, may be irritating and could cause a phenotypic dermatitis without an actual allergy present, resulting in misdiagnosis and unnecessary precautions.[12] In the case of nickel, on the other hand, some individuals may react to as little as 1 ppm although it is screened for levels at 2500–5000 ppm. It is therefore important to identify exquisitely sensitive individuals to inform them that even minimal and transient nickel exposure may produce dermatitis. Testing with serial dilution permits the determination of just how allergic patients are. Understanding the concentration of an allergen needed to produce ACD in the majority of sensitized people is of obvious importance to the cosmetic and personal care industry when developing formulations composed of various ingredients.

Allergen + irritant: Many allergens are marginal irritants as well, resulting in positive-appearing patch tests despite the lack of true chemical intolerance. Examples include formaldehyde, wool wax alcohol (lanolin), paraben mix and carbamate. Occlusion also enhances the irritancy potential of some allergens.[13] Future patch test designs should therefore aim to identify methods of demonstrating allergenicity without false positives due to irritation. Advances in dermatopharmacokinetics could be utilized in this endeavor.[14, 15]

False negative patch test results: How does one explain the phenomenon of the patient who is clinically intolerant in a manner suggestive of ACD but is patch-test negative to the given allergens? One possible explanation is a false-negative result, presumably related to too low a concentration or to an inappropriate vehicle.[16, 17] A systematic investigation of the maximal nonirritant concentration may help to resolve this clinical dilemma.

Special series: As noted, how one examines the data obtained by patch testing also is of critical importance, and in this regard, special series deserve mention. Special series, i.e., materials used in special circumstances such as by hairstylists or metal workers, include everything from photographic chemicals to hair dyes and textiles. Yet with the exception of the acrylate series, the development of special series tests is inadequately evidence-based. Thus, positive results may not correlate with clinical relevance, and valuable allergens may be left out while low-yield allergens are included. One solution to this may be cooperative groups working to determine which allergens should make their way to special series.[18] In addition, clinical relevance deserves emphasis. There is certainly a place for scientists and researchers from the cosmetic and personal care industry, as several of these special series deal with applied personal care/cosmetic products.

Enhanced MSDS Legislation

Besides improvements to patch testing, improved material safety data sheet (MSDS) legislation targeting the issue of secrecy regarding the ingredients of pharmaceutical, cosmetic and consumer products would be beneficial. Currently, if an allergen is less than 1% of a product, it does not require disclosure. Correcting this on a global scale, e.g., listing all chemicals, major synonyms and semiquantitative compositions, will aid researchers as well as patients. In the interest of public health, this area needs leadership, i.e., a person or group that can fight for full disclosure of ingredients. This goal has been accomplished for cosmetic labeling and should be extended to other product arenas.

ACD Analytics

In addition to imperfect test measures, the industry has incomplete knowledge of the chemistry of product allergies. In North America, the only chemical identification procedure commonly performed for ACD is the spot test for nickel, and patients with a patch-proven nickel allergy may use the spot test to determine if a piece of jewelry releases clinically significant nickel. An analytical chemistry center similar to those led by M. Bruze in Sweden, A. Lauerma in Finland and T. Menne and colleagues in Denmark is desperately needed[19–21] to determine whether products that appear to be causing allergic reactions contain certain chemicals or quantities when they are not stated clearly on the product.

Contact Allergy Certification and Fellowship

Beyond analyses and tests, a certification program for researchers conducting patch testing is also proposed. Currently, in the United States, any physician can patch-test and prick-test allergy patients without specialized training; in fact, the United States may be one of the weaker Western nations in terms of patch-test training. However, certification in contact allergy could provide a partial solution. Funding for such a program could come from a number of sources, from the National Institute for Occupational Safety and Health, industry, and the American Academy of Dermatology (AAD), to the Personal Care Products Council, the

[a] *The TRUE test is a design of Allerderm, Petaluma, California, USA.*

International Fragrance Association, and trade groups and unions. Stipends for such a fellowship could range from US $25,000 to $50,000 per year, an investment that should rapidly provide societal dividends. Until a higher standard of clinical care and investigation in contact allergy is achieved, many patients will not be well-served by personal care products.

World Wide Web

Finally, since the World Wide Web is an invaluable source, it holds endless possibilities for ACD. It could be used to focus on international allergen alternatives for health care workers and patients, or to bring together contact dermatitis groups—e.g., the International Contact Dermatitis Research Group, the North American Contact Dermatitis Group, and the European Environmental Contact Dermatitis Research Group, for collaboration in ACD management.[22]

Continuously updated databases of allergens and diagnostic methodologies should be made available to all. Furthermore, groups should continue to work to correct discrepancies, including different concentrations of the same allergen used in tests. Special interest groups may be formed for examining various allergens, including metals, preservatives, etc. There is clearly a place for the cosmetics and personal care industry in this electronic landscape, and cooperations between industry, medical researchers and contact dermatitis groups would provide the most optimal outcomes for consumers and patients.

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