

CONTACT ALLERGY AND IRRITATION FROM PRESERVATIVES

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Synopsis

The use concentration of preservatives in topical products is generally in the range of 0.01% to 1%. Owing to their inherent reactivity, many of these chemicals can induce allergic contact dermatitis and occasionally irritant contact dermatitis. An overwhelming number of preservative formulations are marketed under various trade names and synonyms. Unfortunately, there is no single source of information regarding the production, import and use of the different preservatives. The present paper focus on 5 topics related to contact allergy and skin irritation caused by preservatives:

- 1) The relationship between predictive test results in animals and man and the clinical experience.
- 2) Routine patch testing with preservatives - ingredient labelling.
- 3) Kathon CG.
- 4) Change in the industry's choice of preservatives. New preservatives bring along new reports on allergic contact dermatitis.
- 5) Quaternary ammonium compounds as irritants.

Riassunto

La concentrazione d'uso dei conservanti per i prodotti di uso topico varia in genere dallo 0,01 al 1%. A causa della loro elevata reattività questi composti chimici possono indurre dermatite da contatto e occasionalmente dermatite irritativa da contatto. Molti conservanti sono catalogati ed elencati con diversi nomi brevettati, presentati spesso anche con sinonimi. In questo lavoro si pongono a confronto cinque problematiche connesse con l'insorgenza di eritemi cutanei o con allergie da contatto provocate dall'uso di conservanti.

- 1) La relazione riscontrata tra i tests predittivi sull'animale e sull'uomo e l'esperienza clinica.
- 2) I patch-test con i conservanti in relazione agli ingredienti riportati in etichetta.
- 3) Kathon CG
- 4) Cambiamenti nell'uso dei preservanti. L'uso di nuovi conservanti comporta la comparsa di dermatite allergica da contatto.
- 5) Gli ammoni quaternari come irritanti.

Preservatives may be defined as chemicals added to cosmetics, toiletries, household products, topical drugs, and aqueous and emulsion systems in industry to prevent them from spoiling. Biocides are chemicals capable of destroying living organisms, they are often used as preservatives and some are used as antimicrobial drugs. Common to these chemicals is their ability to interfere with certain chemical reactions and/or with the growth of molds, fungi, bacteria or parasites. The concentration used for preservatives in the finished products is generally in the range of 0.01% to 1%.

These reactive chemicals can induce allergic contact dermatitis, hence they are often included when dermatitis patients are patch tested.

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Predictive tests with biocides related to the clinical experience:

There are examples of biocides with a strong sensitizing potential in predictive allergy test in animals - but giving a low incidence of allergic contact dermatitis during practical use. Chlorocresol was a strong sensitizer in the guinea pig maximization test with a frequency of positive reactions ranging from 15% to 84% of the animals tested, depending on the concentration used for induction. Interestingly, the use of chlorocresol as a preservative in topical corticosteroids is extensive, and in spite of that, clinical chlorocresol allergy occurs only sporadically (1).

Cyttox 3522, containing 10% methylene-bis-thiocyanate, and equivalent products are used as biocides in industrial water systems. Cyttox

3522 sensitized all animals in the guinea pig maximization test. In spite of that, human sensitization has not yet been reported. These two chemicals represent examples of strong experimental allergens used in the environment but which cause only few cases of clinical contact allergy.

On the other hand, there are biocides with a lower sensitizing potential, which provoke a significant number of contact allergies, probably due to widespread use, often in higher concentrations.

The parabens are moderate to weak experimental sensitizers. They are widely used and about 6000 of 19000 cosmetic formulations in the United States are preserved with parabens. Paraben allergy occurs with a frequency around 1% in patch test materials, which justifies the inclusion of parabens in the standard series for patch testing. Among 8000 patients tested at Gentofte from 1971 to 1986 0.8% of females and 1.2% of males were paraben sensitive (2). Earlier, when parabens were used in higher concentrations as antifungal agents - paraben sensitivity was more frequent. Edman and Möeller (3) and Gollhausen and co-workers (4) both found an increasing frequency of paraben sensitivity over the years among their eczema patients subjected to patch testing. Animal data with the parabens show a low sensitization rate. Goodwin (5) failed to sensitize with ethyl-paraben using the guinea pig maximization test. Maurer (6) used the optimization test and sensitized 3-4 of 20 guinea pigs to methyl-paraben - and none of 20 to propyl-paraben using epicutaneous challenge, while 10 to 20 reacted following intradermal challenge.

The predictive test data cannot stand alone but must be evaluated in relation to diagnostic patch tests and the exposure situation.

Routine patch testing with preservatives - ingredient labelling.

The Danish contact dermatitis research group tested a number of biocides on consecutive eczema patients in 1983-1984 (7). Some positive reactions were found, but they were of limited clinical value, because the results were frequently inexplicable. In most cases it was not possible to determine if the reaction was a false positive patch test or if it was an allergic reaction, where exposure to the allergen was not traced. In a recent review on the recommended patch test concentration for preservatives it was striking that for 21 of 34 chemicals it was not possible - on the published data - to give a firm recommendation (8).

This is an argument for the demand for labelling the biocide content on all products, in order to make it easier to choose the appropriate biocides for testing of the patients.

Kathon CG (Cl+me-isothiazolinone) MCI/MI).

MCI/MI is, of course, very much in focus - due to its widespread use and the occurrence of contact allergy to the compound. The active ingredients in Kathon CG, chloromethylisothiazolinone and methylisothiazolinone are strong experimental sensitizers (9-10). The allergen is now included in the standard series and the patch test concentration is currently 100 ppm in aqueous solution. This is a compromise and 200 ppm may yield more relevant positive reactions (11). The MCI/MI story is still not complete and more details are to be expected. A recent European multicentre study revealed that 3% of routinely patch tested eczema patients were positive to MCI/MI with a great variation in the frequency between the 22 centres (12).

Change in the industry's choice of preservatives.

The choice of preservatives in the cosmetic industry is interesting to follow. Unfortunately, the figures are published with a considerable delay; the latest figures are from 1984 (13). Besides Kathon CG, Germall 2 and DMDM hydantoin are used in increasing amounts and subsequently reports on contact allergy to these new preservatives have appeared in the literature (14-15). New preservatives are followed by new reports on allergic contact dermatitis (16).

Quarternary ammonium compounds as irritants.

Irritant dermatitis from preservatives is probably very rare as the use concentrations used are so low. However, some preservatives may be added in higher concentrations to the product to yield an antimicrobial effect. An udder ointment marketed in Denmark was significantly more irritating than alternative skin care products in a chamber-scarification test on volunteers, due to a high content of benzalkonium chloride (17).

In conclusion a better understanding of preservative contact allergy requires:

- 1) a balanced view about the results of the predictive allergy test and dose-response determinations, 2) information about biocide consumption and distribution, and 3) labelling of biocide content in the products. The quotation from Theophrastus Paracelsus is still pertinent: "Alle Ding sind Gift un nichts ohn' Gift. Allein die Dosis macht, dass ein Ding kein Gift ist".

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