

Case report

Mercurochrome allergy. Immediate and delayed hypersensitivity

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We describe eight patients suffering from Mercurochrome allergy. Patch and prick tests were carried out with the following organic and inorganic mercury compounds: thimerosal, Mercurochrome, phenylmercuric acetate, phenylmercuric nitrate, metallic mercury, and mercuric chloride, and with sodium fluorescein. Two patients had an anaphylactic reaction a few minutes after application of Mercurochrome. The prick tests with Mercurochrome were positive and they were negative with the other tested products. All patch tests were negative. In the other six patients, the clinical picture was local eczema, and the patch tests were all positive with Mercurochrome and the inorganic mercuric derivatives. Positive patch tests with thimerosal were found only in two patients, and only one had a positive patch test with salts of phenylmercury. In four patients, the prick test with Mercurochrome, negative in immediate reading, gave a late eczematous reaction.

Key words: cross-reactivity; delayed hypersensitivity; immediate hypersensitivity; Mercurochrome; mercury allergy.

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Mercurochrome (MCCH), a 2% solution of merbromin, which is a disodic salt of dibromohydroxymercurifluorescein, is an organic mercurial antiseptic used throughout the world. It is not related to chrome (metal); in fact, its name comes from the Greek word "chrōma" meaning color. Many cases of delayed hypersensitivity (type IV) to MCCH have been described (1–5), but immediate hypersensitivity (type I) is rarely described (6–10). Both types have been found in the same patient (6, 9, 10). Cross-reactivity between organic (thimerosal, MCCH, phenylmercuric salts) and inorganic mercurials (metallic mercury, mercuric chloride, yellow oxide mercury) may occur (11) but is inconstant for all of them (1–3, 6, 9, 12–15). This study aimed to describe eight patients suffering from MCCH hypersensitivity (two of type I and six of type IV) in order to determine the differences between them and what mercury compounds they were sensitized to.

Material and methods

Eight patients showing some adverse reactions after topical application of MCCH antiseptic solution in skin injuries were studied.

Case reports

Patient 1. A 29-year-old woman had suffered 7–8 episodes of intense pruritus in the scalp, generalized erythema, angioedema of the eyelid, sensation of a foreign body in the throat, and dyspnea a few minutes after application of MCCH in the anal cleft. These symptoms disappeared a few hours after administration of antihistamines and corticosteroids.

Patient 2. A 38-year-old woman twice developed generalized urticaria and angioedema, dyspnea, wheezing, and abdominal pain a few minutes after application of MCCH to a wound. The clinical signs became normal a few hours after administration of antihistamines and corticosteroids.

Patient 3. A few months before the study, a 4-year-old boy developed a local eczematous eruption 2 h after the application of MCCH to a wound on his leg. The eczema spontaneously healed after several days with desquamation.

Patient 4. A 7-year-old girl developed local vesicles 12–18 h after application of MCCH. They resolved

after 1 week with desquamation. A silver amalgam dental filling was removed because it caused gum-boil.

Patient 5. A 13-year-old boy developed generalized acute dermatitis (baboon syndrome) twice 18 h after inhaling vapor of metallic mercury during a practical class at school. He had a history of local eczema after topical application of MCCH. This case has been reported extensively (16).

Patient 6. An 18-year-old man showed local skin eczematous lesions 10–12 h after application of MCCH.

Patient 7. A 4-year-old girl showed local skin eczematous lesions 6–8 h after application of MCCH.

Patient 8. An 11-year-old girl showed local skin eczematous lesions 6–8 h after application of MCCH. She also had contact dermatitis caused by wax pictures, Plasticine, and black jeans. We performed patch tests (PT) with the Spanish standard, textile and dye series (J. Martí Tor, Barcelona, Spain), finding positive PT only with metallic mercury and thimerosal.

The vaccines containing thimerosal as preservative were well tolerated by all eight patients.

Allergologic study

All the patients were patch-tested with the following organic and inorganic mercury compounds: thimerosal 0.1% pet., MCCH 2% aq., phenylmercuric acetate 0.01% aq., phenylmercuric nitrate 0.01% aq., metallic mercury 0.5% pet., and mercuric chloride 1% aq., all provided by J. Martí Tor, Barcelona, Spain. We also carried out PT with sodium fluorescein 2% aq. (Colircusi fluoresceína®, Laboratorios Cusí SA, Barcelona, Spain). PT were carried out on the back with Leukotest®

(Beiersdorf AG, Hamburg, Germany). The PT readings were conducted according to International Contact Dermatitis Research Group guidelines after 2 and 4 days. If significant reactions occurred before, we read them immediately. Skin prick tests (SPT) were performed on forearms with the same products referred to before and in the same presentation. The longest and perpendicular diameters of the wheal were measured at 15 min, and patients were informed that if a late reaction developed, they must return to us for examination. The positive control was histamine (10 mg/ml).

Results

The SPT were positive, in immediate reading, only in patients 1 and 2 and exclusively with MCCH, patient 1 showing a wheal of 10×6 mm (histamine 5×5) and patient 2 a wheal of 10×5 (histamine 8×5). In patients 4, 5, 6, and 7, the SPT with MCCH, negative in immediate reading, gave a late eczematous reaction, patient 5 showing an intensive eczematous reaction at 12 h and the others at 24 h. We also saw a late eczematous reaction with SPT in patient 5 to metallic mercury and mercuric chloride (both intensive reactions at 12 h) and in patient 8 with mercuric chloride at 24 h.

Table 1 shows the PT results.

Discussion

MCCH can produce allergic reactions of immediate type. In all six cases described in the literature (6–10) that we reviewed, positive SPT with MCCH was found, but in only one of them was positive SPT with thimerosal found (8). Two of our eight patients (patients 1 and 2) had symptoms of anaphylactic reaction a few minutes after MCCH was applied to an injury. Both the SPT with MCCH at the 2% concentration were positive, but negative with the other mercury compounds. We carried out SPT with fluorescein because MCCH is a mercuric

Table 1. Results of patch tests with mercury derivatives and fluorescein in eight patients studied

Patients	Metallic mercury D2/D4	Thimerosal D2/D4	Mercuric chloride D2/D4	Mercurochrome D2/D4	Ph-Hg Acet D2/D4	Ph-Hg Nitrat D2/D4	Fluorescein D2/D4
1	–/–	–/–	–/–	–/–	–/–	–/–	–/–
2	–/–	–/–	–/–	–/–	–/–	–/–	–/–
3	+ +/+ + +	+/?	+ + +/+ + +	+ +/+ + +	–/–	–/–	–/–
4	+ + +*/+ + +	–/–	+ + +*/+ + +	+ + +*/+ + +	–&/–	?&/–	–/–
5	+ +/+ + + +	+ +/+ + +	+ +/+ + +	+ +/+ + + +	–/–	–/–	–/–
6	+ +*/+ + +	–/–	+ + +&/+ + +	+ +*/+ + +	–/–	–/–	–/–
7	+ +/+ + +	–/–	+ + +&/+ + +	+ + +&/+ + +	+/+	+/+	–/–
8	+ +*/+ + +	+/+	+ + +*/+ + +	+ +/+ + +	–/–	–/–	–/–

Ph-Hg Acet: phenylmercuric acetate; Ph-Hg Nitrat: phenylmercuric nitrate; D2 and D4: readings of patch tests at 48 and 96 h; ?: doubtful reaction; #: + + at 24 h; &: + at 24 h; \$: + + + at 24 h; *: + + at 6 h.

fluorescein compound; they have a very similar chemical structure, and MCCH contains within its structure the whole fluorescein molecule (Fig. 1). In both patients, SPT with fluorescein was negative. This lack of cross-reactivity was also found by other authors (6, 10, 17). The immediate hypersensitivity to MCCH is due to an IgE-mediated mechanism, and it has been demonstrated by positive passive transfer test (PK) (8, 9). Specific IgE against MCCH has not been found (6, 7).

Of the six cases of type I allergy to MCCH reviewed (6–10), three also shared a type IV mechanism with positive PT with MCCH and other mercury compounds (6, 9, 10). None of our patients with type I allergy to MCCH showed positive PT, indicating that the mechanism responsible for their hypersensitivity was exclusively type I.

Type IV allergic reactions with MCCH have been described more frequently (1–5, 16). Generally, they tend to cause local eczema but they can also be manifested as generalized eczema (3, 4). All six patients with delayed hypersensitivity to MCCH described by us showed only local reactions, these reactions generally beginning 6 h after the application of MCCH, but patient 3 showed the reaction after 2 h. The young age of our patients who showed delayed reactions is striking; their ages ranged between 4 and 18 years ($xL=9.5$). The mercury compounds allergy is common in children (1, 2, 6, 12, 14); in Spanish children, mercuric chloride is the third most common cause of contact dermatitis after nickel and rubber compounds (18). The early appearance of this reaction can be explained by the frequent use of MCCH as an antiseptic in children.

Cross-reactivity between organic and inorganic mercury compounds may occur (11), but it is inconsistent for all of them. In 15 patients complaining of baboon syndrome from mercury, Nakayama et al. (15) found positive PT with nearly all the mercury compounds, these being more intensive and persistent with inorganic derivatives (metallic mercury, mercuric chloride, and mercury ammonium). In other reports (1–4, 6, 9, 12–14), positive PT with most mercury compounds are described, but they were less persistent with thimerosal and salts of phenylmercury, while there were no negative PT with inorganic derivatives. In this study, we found that the six patients with type IV hypersensitivity from MCCH had positive PT with the inorganic derivatives tested (metallic mercury and mercuric chloride). Positive PT with thimerosal were found only in two patients, and only one had a positive PT with salts of phenylmercury. These data agree with findings in the literature.

Mercuric chloride can produce irritative reactions (11), but we think that our patients showed true sensitization since they were also positive to

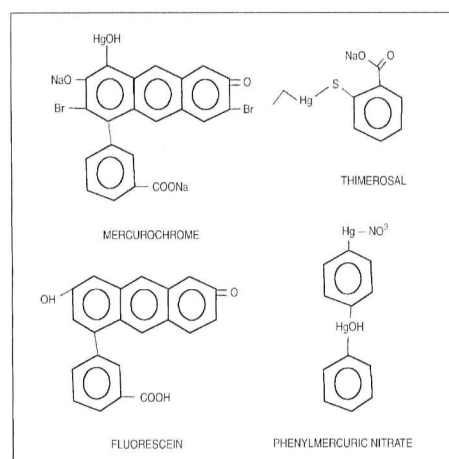


Fig. 1. Chemical structure of several mercury derivatives and fluorescein.

other mercury compounds. In four patients, we found important reactions at 24 h (D1) with MCCH, metallic mercury, and mercuric chloride. In one of them (patient 8), there was even an intensive reaction (+++) at 6 h. We do not know whether the other two patients had early reactions since a reading was only made at D1 if the patient came to our consultancy with irritation. It is striking that in four patients (patients 4, 5, 6, and 7), the SPT with MCCH, negative in immediate reading, gave a late eczematous reaction. We also saw this phenomenon in a patient (no. 5) with metallic mercury and in two (nos. 5 and 8) with mercuric chloride. We have not seen this phenomenon described with MCCH in the literature, but it is not uncommon with other drugs such as penicillin (21).

Like Barranco et al. (6), we think that in the case of immediate allergy from MCCH, the antigen responsible is the whole molecule, since these patients have positive SPT almost exclusively with this product, and not with other mercury derivatives. In the case of delayed allergy, the mercury ion is responsible since the PT are positive with several mercury compounds.

Patients with type IV allergy from MCCH must avoid contact with products containing mercury. Our patient no. 4 had to remove a silver amalgam dental filling that gave her a gumboil, and it cannot be ruled out that it was the result of a hypersensitivity reaction to amalgam. Patient no. 5 developed two episodes of generalized eczema after inhalation of mercury vapor. Patient 8 showed cutaneous eczema with black jeans, wax pictures, and Plasticine, and some of these products are known to contain mercury derivatives as preservative. In 15 patients with baboon syndrome from mercury, Nakayama et al. (15) found that 11 showed previous MCCH allergy. For patients with type I allergy from MCCH, it is

probably not necessary to avoid other mercury derivatives, with the exception of mercuric fluorescein compounds, but, given the intensity of some reactions, it is advisable to avoid them all.

The meaning of the positive PT with thimerosal is uncertain since there are cases of positive PT with good tolerance of vaccines that contain it as a preservative (19), and there are also known cases of cutaneous reactions after vaccines with positive PT with thimerosal (20). We found positive PT in only two cases, and it was doubtful in another; however, all eight patients tolerated the vaccines.

In conclusion:

- 1) In an adverse reaction from MCCH, SPT and PT with a battery of organic and inorganic derivatives of mercury should be carried out, since a type I or IV mechanism or both may be involved.
- 2) PT should be read at D1 and SPT at 15 min and 24–48 h (it may give an isolated late reaction).
- 3) When there is allergy to MCCH (type I or IV), all derivatives of mercury should be avoided.

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