

Contact Urticaria from Carboxymethylcellulose in White Chalk

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Background: Carboxymethylcellulose (CMC) is widely used in consumer goods, foods, and medicaments as a binder, emulsifier, and viscosity enhancer. Cases of immediate and delayed allergic reactions to this anionic cellulose polymer have been reported.

Objective: To report a case of contact urticaria from CMC in chalk, with possible cross-reaction to methyl hydroxyethylcellulose (MHEC).

Method: Patch tests with readings at 48 and 96 hours were performed with the North American Contact Dermatitis Group standard series and benzisothiazolinone. Open and prick tests with readings after 30 minutes were performed with two brands of chalk as well as with various petrolatum and aqueous dilutions of CMC, MHEC, oleic acid, and calcium carbonate.

Results: The patient developed strong urticarial reactions during open tests with both powdered chalks and had milder reactions to the open test with CMC 10% aqueous (aq) and to prick testing with CMC 0.1% aq. No reaction to MHEC or any of the other ingredients of the chalks was observed. No relevant delayed reaction was noted.

Conclusion: CMC can cause contact urticaria. It remains unclear why our patient reacted more strongly to the chalk than to CMC itself. We speculate that the abrasive nature of the chalk enhances the cutaneous penetration of CMC or that calcium carbonate, the main ingredient of the chalk, acts as an adjuvant. It is also possible that CMC and MHEC cross-react and that our negative results with MHEC may be due to improper testing technique or concentrations.

SODIUM CARBOXYMETHYLCELLULOSE (CMC) is an anionic cellulose polymer that is synthesized from cellulose and sodium chloracetate (Fig 1).¹ It is used as

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The Patch Test Clinic will publish articles directly related to patch testing. The format is a short report including abstract, introduction, materials and methods, discussion, and references. Relevant tables and figures are encouraged.

a binder, emulsion stabilizer, and viscosity enhancer in numerous preparations. Because of its large molecular size, it should be poorly absorbed through the skin or gastrointestinal tract and thus should exhibit a low potential for the development of allergic reactions. Nevertheless, it has been identified as an allergen in a wide range of preparations. It has caused anaphylactic reactions from corticosteroid injections²⁻⁵ and barium sulfate suspensions⁶ and has elicited contact urticaria from hydrocolloid dressings.⁷ In addition, a case of contact dermatitis from CMC has been described in a baker.¹ We report a case of contact urticaria from CMC in white chalk, an unusual and previously undescribed source of exposure.

Case Report

A 17-year-old female student was referred to our patch-test clinic for evaluation of immediate pruritus and localized edema after contact with the powder of white or colored chalk. She had a history of childhood asthma, atopic dermatitis, and allergic rhinitis. The actual problem began in early November 2002, with episodes of erythema, swelling, and intense itching a few minutes after she had handled chalk or from contact with the fingers of someone who had handled chalk. According to the patient, the lesions evolved into "blisters" a few hours after the initial contact and healed with pigmentary changes. She consulted an allergist, who was able to elicit an immediate urticarial reaction to powdered white Crayola chalk (Binney & Smith, Easton, PA) applied to her forearm without occlusion.

The manufacturer obligingly disclosed the composition of the chalk, which is 95 to 98% calcium carbonate.

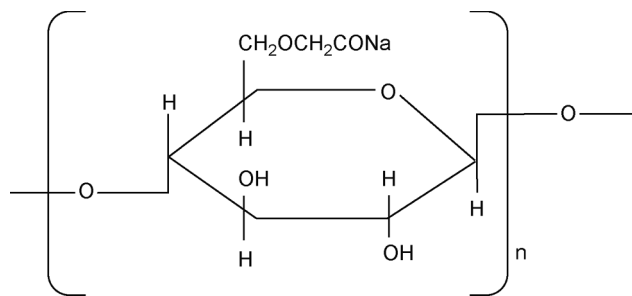


Figure 1. Chemical structure of carboxymethylcellulose.

Other ingredients include CMC (as a binder) and the preservatives benzisothiazolinone and 5-chloro-2-methyl-4-isothiazolinone/2-methylisothiazolinone (MCI/MI). In addition, colored chalk contains 1.5% (by weight) of pigment dispersion.

Patch testing was done with the North American Contact Dermatitis Group standard series, which contains MCI/MI, and we included benzisothiazolinone 0.05% in petrolatum (Chemotechnique Diagnostics, Malmö, Sweden), applied with Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) on Scanpor tape (Norgesplaster A/S, Venesla, Norway). Readings were performed after 48 and 96 hours. The patient had positive reactions to nickel (++), fragrance mix (+), and cinnamic aldehyde (+), which were deemed of past relevance. She had no reaction to the isothiazolinones.

We tested the other ingredients of the chalk by the open and prick-test techniques. These tests were performed in a standard fashion on the volar aspect of the right forearm that had never been exposed to the chalk. CMC was tested at 10%, 5%, and 2.5% in petrolatum (pet) as well as at 10%, 1%, and 0.1% in an aqueous solution (aq). We also tested with calcium carbonate 2.5 % pet and with two brands of white chalk from two different manufacturers, “as is”: Crayola (Binney & Smith) and Prang (Dixon Ticonderoga, Heathrow, FL). Readings were done at 30 minutes after application (Table 1). Positive reactions were noted in the open test with CMC 10% aq and in the prick test with CMC 0.1% aq. However, the open test with powdered chalk gave rise to the strongest reactions, obviating the need to perform prick tests with this substance. Because the patient had a positive reaction to Prang chalk, we contacted the manufacturer and learned that Prang chalk contains (along with calcium carbonate and oleic acid) methyl hydroxyethylcellulose (MHEC) instead of CMC as a binder. The patient was also tested with these additional substances, with negative results. None of the sites of the open and prick tests de-

veloped late reactions. We believe that the “blisters” and pigmentary changes described by our patient were the results of vigorous scratching.

The patient was warned against further exposure to CMC and was doing well. A few months later, however, during a visit to the dental hygienist, she developed a burning sensation of the gums within 5 minutes of the application of a pumice cleanser called Nupro Prophylaxis Paste (Dentsply, York, PA). The paste was immediately removed, but in the following hours, the patient developed tenderness and edema of the gums that resolved with desquamation in about 1 week. The manufacturer of the paste revealed that it contains CMC. This information does not appear in the list of ingredients on the package insert.

Discussion

CMC enjoys a wide range of applications in various commodities and medical preparations. Its hygroscopic properties and high solubility make it an ideal thickener, viscosity enhancer, and emulsifier. CMC can be found in ice creams, toothpastes, candies, canned and frozen foods, jams, and instant noodles. It is also used in textile sizing, in paper processing, and in detergents, adhesives, latex paints, and polishes. Medical products in which CMC is used include hydrocolloid dressings, bulk laxatives, gastric antacids, barium radiocontrast media (for gastrointestinal series), artificial tears, dental prosthesis adhesives, viscous

Table 1. Results of Initial Testing

Substance Tested	Open Test*	Prick Test*
CMC 10% pet	—	—
CMC 5% pet	—	—
CMC 2.5% pet	—	—
CMC 10% aq	10 mm flare	—
CMC 1% aq	—	—
CMC 0.1% aq	—	15 mm flare, 10 mm induration
Calcium carbonate 2.5% pet	—	—
Calcium carbonate “as is”	—	—
Prang white chalk “as is”	5 cm flare, 10 mm induration	Not done
Crayola white chalk “as is”	4 × 6 cm urticarial reaction	Not done

aq = aqueous; CMC = carboxymethylcellulose; pet = petrolatum.

*Reading at 30 minutes.

lidocaine (Xylocaine, AstraZeneca, London, UK), and injectable hydrophobic medicaments such as corticosteroids and hormones, in which it serves as a suspending agent and solubility enhancer.³ It is used as binder in tablets and in other materials, such as cosmetics, that require caking of powdery material. CMC renders chalk dustless and less friable.

Reported cases of immediate reactions to CMC were documented through positive prick-test results. Our patient, however, developed immediate reactions to open tests with the chalk itself and with CMC 10% aq. Her prick-test results were also positive for CMC 0.1% aq but were (surprisingly) negative for higher concentrations. Other ingredients of the chalk gave negative reactions, making CMC the most likely allergen. The fact that the patient reacted to open tests implies that absorption occurs through intact skin. We cannot readily explain why her reactions were stronger with the chalk than with pure CMC. We hypothesize that absorption may be increased by the abrasiveness of calcium carbonate. Alternately, calcium carbonate may act as an adjuvant that increases immunologic reactivity against CMC. Finally, it is possible that CMC may be structurally or chemically modified in the chalk so as to give rise to a more allergenic molecule; this phenomenon would be similar to "compound allergy" wherein cell-mediated reactions to a compound occur whereas the results of patch tests with its separate ingredients are negative.

We are unaware of the actual concentration of CMC in the chalk, but from information obtained from the manufacturer, we can assume that it is less than 5%. We therefore elected not to expose our patient to pure CMC, either in open tests or in prick tests. Instead, we used various dilutions in water and petrolatum, as suggested by a search of the available literature. In view of our results, it would appear that the best medium for testing is water.

Our patient reacted to Prang chalk but did not react to MHEC, the filler used in this brand of chalk. MHEC may still be responsible for our patient's reaction to the chalk, and our failure to demonstrate it could have resulted from improper testing technique or improper concentration; despite vigorous agitation, our solution of MHEC remained viscous and appeared nonhomogeneous. The same phenomenon may explain the discrepancy between our patient's reactions to high and low concentrations of CMC.

We raise the possibility that CMC and MHEC cross-react. Both CMC and MHEC belong to the cellulose ether family, whose compounds are formed by substituting some of the cellulose hydroxyl groups. CMC belongs to the ionic cellulose ether group whereas MHEC is a non-ionic cellulose ether, soluble in cold water. The non-ionic cellulose ethers (which also include methylcellulose and methylhydroxypropyl cellulose) are used in bonding plaster, finishing mortar, fillers, tile adhesives, and finishing coats based on synthetic resin. They are used in tobacco sheets, in adhesives for cigarette paper and cigar seams, in laundry detergents, and in medical plaster bandages. Non-ionic cellulose ethers are also used as viscosity enhancers in enamels and ceramic glaze; binders in pencils and crayons; gelatinizing agents; thickeners in printing inks; textile coatings; and thickeners in cosmetics, toothpaste, shampoos, and soaps.

Our case demonstrates that CMC is a potential allergen that can trigger contact urticaria. It emphasizes the need for awareness or for mandatory listing of ingredients on the labels of apparently inoffensive consumer goods. We advised our patient to carefully read the ingredient lists of foods that may contain CMC. We also made her aware of the various sources of exposure from medical devices or drugs.

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