

Occupational periorbital allergic contact dermatitis caused by antioxidants in black rubber in an otorhinolaryngologist using an otomicroscope

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Allergic contact dermatitis caused by rubber accelerators is common. However, antioxidants in black industrial rubber are also important causes of occupational allergic contact dermatitis (1–6). The antioxidants discolour the rubber, and are therefore primarily used in black

rubber to stabilize the product and to make it resistant to oxidation, heat, ultraviolet light, etc. If the TRUE Test[®] is used, contact allergy to black rubber chemicals can be diagnosed with the black rubber mix chemicals, namely *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine (IPPD), *N*-cyclohexyl-*N'*-phenyl-*p*-phenylenediamine and *N,N'*-diphenyl-*p*-phenylenediamine. These are all commonly used as antioxidants in the production of industrial black rubber products. IPPD is also present as a pet.-based allergen in the European baseline series as a single compound.

Here, we report an unusual occupational case of allergic contact dermatitis caused by black rubber antioxidants in a physician using an otomicroscope with a black rubber cuff on the ocular piece.

Case Report

A 59-year-old physician working as an otorhinolaryngologist referred himself because of a recurrent and symmetrical eczematous rash in the periorbital area. He had no personal history of atopy. The dermatitis developed after the acquisition and use of a new otomicroscope in the practice, and allergic contact dermatitis caused by black rubber in the ocular pieces was suspected. The patient presented with a slight papular eczematous rash around the eyes, but he showed pictures of rather severe periorbital eczema (Fig. 1). When he decided to use his old otomicroscope again, the eczema quickly resolved.

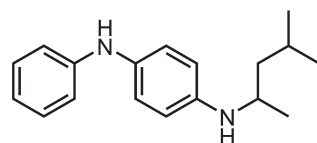
The patient was patch tested with the European baseline series, the rubber gloves used in his clinic (latex gloves), and the moisturizing creams and glucocorticoid cream Locoid[®] (hydrocortisone 17-butyrate) 'as is' that he had used briefly for treating the eczema. The patch test materials were applied to the back for 2 days with TRUE Test[®] panels 1–3 (SmartPractice Aps, Hillerød, Denmark), and Finn Chambers[®] on Scanpor[®] tape (SmartPractice, Phoenix, AZ, USA) were used for the remaining test preparations. Readings were performed on day (D)4. The concentrations and positive reactions are shown in Table 1. Efforts were made to obtain a list of chemicals used in the black rubber from the company that had imported the otomicroscope, and also from the factory itself. Unfortunately, the only compound that could be identified was the antioxidant *N*-(1,3-dimethylbutyl)-*N'*-phenyl-*p*-phenylenediamine (6-PPD). However, the patient was not tested with this substance, because it was not commercially available, but with the two related antioxidant rubber allergens, namely IPPD and *N*-cyclohexyl-*N'*-phenyl-*p*-phenylenediamine (Fig. 2). The reaction to neomycin was not of current relevance.



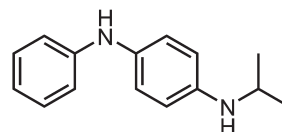
Fig. 1. The periorbital eczema in the patient after use of the otomicroscope.

Table 1. Test results for the D4 readings

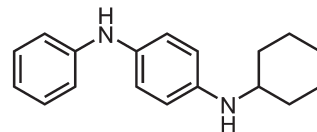
Test substance	Concentration	D4
Neomycin	200 µg/cm ²	+
Black rubber mix	75 µg/cm ²	++
<i>N</i> -isopropyl- <i>N'</i> -phenyl- <i>p</i> -phenylenediamine	0.1% pet.	++
<i>N</i> -cyclohexyl- <i>N'</i> -phenyl- <i>p</i> -phenylenediamine	1% pet.	++



N-(1,3-Dimethylbutyl)-*N'*-phenyl-*p*-phenylenediamine (6-PPD)



N-Isopropyl-*N'*-phenyl-*p*-phenylenediamine (IPPD)



N-Cyclohexyl-*N'*-phenyl-*p*-phenylenediamine

Fig. 2. Chemical structures of allergenic black rubber antioxidants.

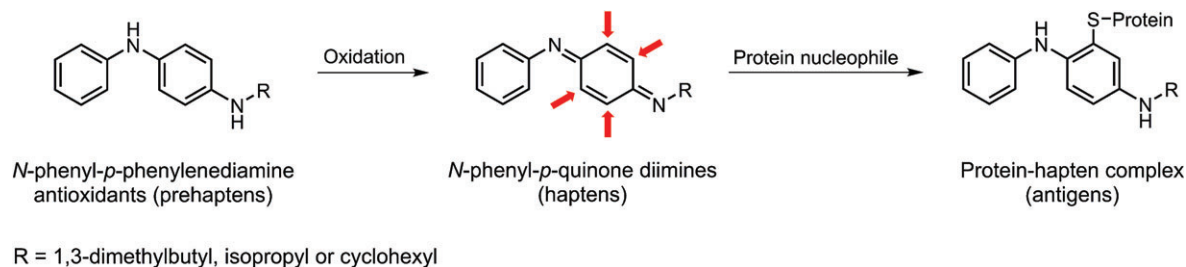


Fig. 3. Haptening of allergenic black rubber antioxidants. Red arrows indicate different active sites on the haptens that are suitable for nucleophilic attack by proteins, generating antigens.

Discussion

We report here a patient history with a clear correlation between the development, and eventual resolution, of the dermatitis and exposure to new equipment with black rubber cuffs. The culprit allergen(s) in this case were indicated by positive patch test reactions to the common black rubber antioxidants IPPD and *N*-cyclohexyl-*N'*-phenyl-*p*-phenylenediamine. Although it was not possible to obtain a complete list of chemicals in the black rubber cuffs, the present case shows that black rubber antioxidants included in the test panel were able to confirm contact allergy.

6-PPD has previously been shown to be a cause of allergic contact dermatitis caused by rubber products (5–8). On exposure to air and light, 6-PPD is easily oxidized to *N*-(1,3-dimethylbutyl)-*N'*-phenyl-*p*-quinone diimine, which makes it a strong reducing agent (antioxidant). Antioxidants related to 6-PPD, such as IPPD and *N*-cyclohexyl-*N'*-phenyl-*p*-phenylenediamine, are also easily oxidized to their corresponding *N*-phenyl-*p*-quinone diimines. This process is most likely abiotic, and occurs

on the skin via air oxidation and/or by non-specific biochemical mechanisms (9); hence, the above-mentioned antioxidants are considered to be prehapten (Fig. 3). The *N*-phenyl-*p*-quinone diimines are highly reactive towards nucleophiles such as thiol groups in proteins, generating protein–hapten complexes (antigens) in the same way as quinones (Fig. 3), which explains why these rubber antioxidants are all expected to be contact allergens. Consequently, 6-PPD, IPPD and *N*-cyclohexyl-*N'*-phenyl-*p*-phenylenediamine generate the same type of haptens following oxidation. Furthermore, these haptens all have the same reactive sites and give rise to the same haptening reactions; hence, cross-reactions are therefore expected between these rubber antioxidants (Fig. 3), in accordance with previous reports (6, 7). In conclusion, the positive reactions observed to black rubber mix, IPPD and *N*-cyclohexyl-*N'*-phenyl-*p*-phenylenediamine clearly indicate that antioxidants in the black rubber cuffs are the causative allergens for the observed allergic contact dermatitis in this patient.

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