

Occupational peri-ocular contact dermatitis due to sensitization against black rubber components of a microscope

D. I. M. KUIJPERS¹, F. HILLEN² AND J. A. FRANK¹

¹Department of Dermatology and ²Department of Pathology, University Hospital Maastricht, Maastricht, the Netherlands

A 24-year-old female working in the Department of Pathology of a University Hospital developed an acute peri-ocular eczema clearly being related to her daily work at the microscope. Patch testing revealed delayed type hypersensitivity against the black rubber mix, *N*-isopropyl-*N*'-phenyl paraphenylenediamine, *N*-cyclohexyl-*N*'-phenyl paraphenylenediamine and the rubber ring situated on the ocular of the respective microscope. This is the first report, to our knowledge, on peri-orbital allergic contact eczema because of sensitization with rubber components of a microscope.

Key words: black rubber mix; contact allergy; contact dermatitis; *N*-cyclohexyl-*N*'-phenyl paraphenylenediamine; *N*-isopropyl-*N*'-phenyl paraphenylenediamine. © Blackwell Munksgaard, 2006.

Accepted for publication 10 March 2006

The term contact dermatitis is commonly used to describe an inflammatory reaction of the skin that is induced by exposure to an environmental agent. The primary clinical manifestation comprises erythema, vesicles and pruritus. Secondary skin lesions may consist of erosions, excoriations, and postinflammatory hyperpigmentation.

Allergic contact dermatitis is caused by small chemical molecules, so-called haptens, which have a molecular weight of less than 500 Da. Because of their small size, these haptens can effectively penetrate the skin barrier that is usually impermeable for large molecules under physiological conditions.

Unavoidable recurrent and longstanding direct contact with potential sensitizers because of work-related circumstances can lead to occupational allergic contact dermatitis. Among those particularly prone to this disease are individuals working in hospitals and health-care professions. Recently, nickel sulfate, disinfectants and rubber components were reported to comprise the most relevant sensitizing agents leading to occupational allergic contact dermatitis among health-care workers (1).

In Europe, putative contact sensitizations are usually confirmed with a patch test using the European Standard contact dermatitis testing

series that, among other test substances, also contains the black rubber mix (2).

Irritant and allergic contact dermatitis account for as much as 90–95% of all occupational skin diseases. The vast majority of patients with occupational contact dermatitis present with hand eczema that can lead to recurrent or permanent inability to work and, eventually, unemployment (3, 4). In the current unusual case, however, a young female working in the Department of Pathology of a University Hospital developed peri-ocular eczema because of her daily direct contact with the rubber-coated surface of a microscope. Patch test results indicated a causative role of substances contained in the black rubber mix in the aetiopathogenesis of eczema in this patient.

Materials and Methods

A 24-year-old female research fellow, working in the Department of Pathology of our University Hospital, developed acute itching ocular skin lesions that had manifested 8 months after having started to work at different microscopes on a daily basis. Several weeks ago, a representative of the department's official microscope dealer

had maintained these microscopes, thereby using alcohol-containing solutions.

The patient's medical history revealed atopic eczema in childhood and a putative allergy for medical tape. However, she had not experienced peri-ocular eczema previously. Family history revealed atopic eczema and delayed type hypersensitivity against nickel sulfate in her father.

At first examination in our outpatient unit, we saw symmetrical, sharply demarcated erythematous macules with slight scaling and swelling that were arranged in a linear pattern and confined to the infra-ocular region (Fig. 1a).

To screen for delayed type hypersensitivities, we performed a patch test with the European Standard contact dermatitis testing series, also referred to as thin-layer rapid use epicutaneous (TRUE) test (Bipharma B.V., Weesp, the Netherlands) and also tested the original rubber rings after removing them from the oculars of the respective microscopes at which the patient worked.

Results

Beside weakly positive reactions against nickel sulfate (+) and perfume mix (+) (data not shown) patch testing revealed hypersensitivities of the delayed type against black rubber mix (+ + +) and the aforementioned rubber rings (+) (Fig. 1b, c). Because the black rubber mix is composed of three substances: (i) *N*-isopropyl-*N'*-phenyl paraphenylenediamine (IPPD) 0.1%, (ii) *N*-cyclohexyl-*N'*-phenyl paraphenylenediamine (CPPD) 0.25%, and (iii) *N*, *N'*-diphenyl paraphenylenediamine (DPPD) 0.25%, we sought to further differentiate the contribution of each single component. Patch testing with IPPD showed

a strongly positive reaction (+ + +) (Fig. 1c), as did CPPD (+ +) whereas the test with DPPD was negative (Fig. 1d).

Discussion

The development of allergic peri-ocular eczema because of long-lasting direct contact with the rubber-coated ocular surfaces of a microscope, as described herein, is a rather uncommon manifestation of an occupational dermatosis.

As an important industrial and consumer product rubber is ubiquitously encountered in many household items and medical devices. In order to reduce the process of perishing (cracking of rubber over time because of exposure to atmospheric oxygen and ozone), antioxidants and antiozonants are added to the rubber prior to vulcanization. In particular, rubber intended for industrial, heavy use, contain such additives that are all derivatives of paraphenylenediamine (PPD).

However, antioxidants and antiozonants causing allergic contact dermatitis can not only be found in rubber used for industrial applications (e.g. tyres, gloves) but also in other products as rubber bracelets and watch straps, scuba masks and swimming goggles, squash balls, motorcycle handles, spectacle chains, eyelash curlers, footwear, orthopaedic bandages or rubber escalator railings (5–11).

Most individuals with putative contact sensitizations against rubber will usually be patch-tested with thiuram mix, carbamates, and the black rubber mix (PPD mix). In a series of 145 patients with confirmed rubber allergy the black rubber mix accounted for as much as 23% of the positive test allergens with thiuram mix being the most frequent sensitizer (68%). More than half of

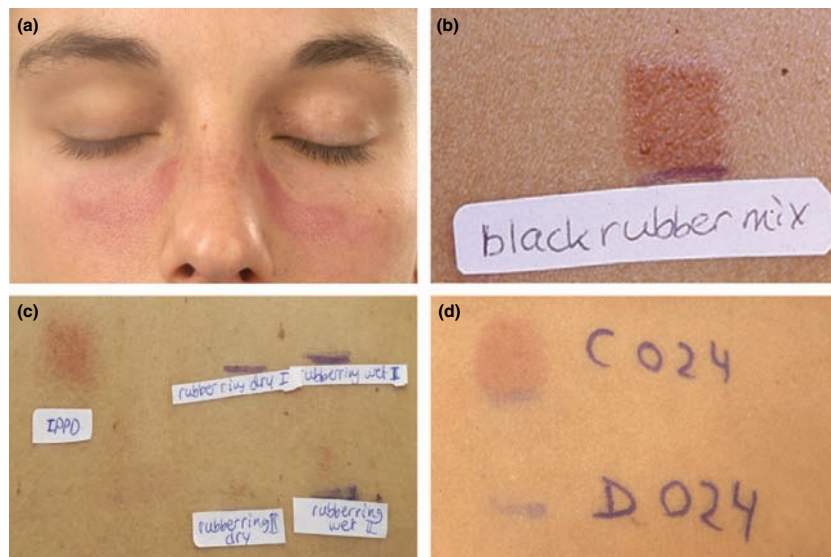


Fig. 1. (a) Peri-ocular eczema. (b) Positive test result on black rubber mix. (c) Positive test result on *N*-isopropyl-*N'*-phenyl-*p*-phenylenediamine as well as one of the rubber rings of the microscope. (d). Positive test result on *N*-phenyl-*N'*-cyclohexyl-*p*-phenylenediamine (c024), negative test result on *N*, *N'*-diphenyl-*p*-phenylenediamine (d024).

these patients had an occupational exposure to rubber leading to sensitization (12).

Although the black rubber mix accounts for a prevalence of 0.6% of all contact allergens contained in the TRUE test (13), some suppliers of the European standard series have stopped producing this mix because of difficulties in the availability of CPPD and DPPD. Instead, the black rubber mix is more and more replaced by IPPD 0.1% because IPPD is considered to be the most important rubber antioxidant causing contact dermatitis (8,14). Of note though, 10% of rubber contact allergies can be missed when testing IPPD exclusively (14).

Interestingly, false negative results after patch testing with the standard series are well documented (15). Therefore, it is mandatory to not only test single components of the black rubber mix as, e.g. IPPD but also, whenever possible, the original rubber-containing products to which the patient has daily contact. Although IPPD, which is predominantly used as hair dye agent, is chemically different from PPD, cross-reactivity between the two substances has been described (16). Because of the sensitization potential of IPPD, *N*-1,3-dimethylbutyl-*N'*-phenyl-*p*-phenylenediamine (DMPPD) is nowadays more and more used as a substitute in the production of black rubber. Unfortunately, many patients allergic to IPPD also test positive for DMPPD (15).

The patient presented herein developed delayed type hypersensitivities against the black rubber mix, IPPD and CPPD, clinically presenting as an acute peri-ocular contact dermatitis. These sensitizations were most likely acquired in the course of her repeated direct daily skin contact with the rubber rings on the oculars of a microscope at work. In support of this argumentation, the patch test performed with one of the rubber rings from the microscopes revealed a positive result and, thus, almost undoubtedly confirmed the causative role of this rubber product and the aforementioned contact allergens in the skin manifestations observed. Although one might wonder if recurrent direct skin contact with the rubber components of the microscope over a period of 8 months is sufficient to develop a contact allergy it is important to consider two further aspects that might have promoted the development of contact sensitization in this particular patient.

First, our patient indicated that she had been a passionate swimmer during adolescence and repeatedly had had contact with black rubber padding on her swimming goggles over many years. This early and repeated exposure to rubber

material might have promoted and accelerated the peri-ocular contact dermatitis.

Secondly, she had a medical history of atopic eczema during childhood and adolescence. Several reports indicate that atopic patients more often suffer from an impaired skin barrier function than healthy individuals and, thus, reveal an increased susceptibility for the development of contact allergies (17, 18). Although we are well aware of the fact that this aspect has been controversially discussed in the past (19), it is tempting to hypothesize that this circumstance likewise might have accelerated the phase of sensitization.

After establishing the diagnosis a topical ointment with triamcinolone acetonide 0.1% resolved the eczema. Today, the patient still works at the microscope that has been equipped with a protective coating of poly tetra-fluoro-ethene (Teflon) to prevent further sensitization. To our knowledge, this is the first report of an occupational skin disease manifesting as allergic peri-ocular contact eczema because of sensitization against rubber components of a microscope.

References

1. Nettis E, Colanardi M C, Soccio A L et al. Occupational irritant and allergic contact dermatitis among healthcare workers. *Contact Dermatitis* 2002; 46: 101–107.
2. Bruynzeel D P, Andersen K E, Camarasa J G et al. The European standard series. European Environmental and Contact Dermatitis Research Group (EECDRG). *Contact Dermatitis* 1995; 33: 145–148.
3. Keil J E, Shmunes E. The epidemiology of work-related skin disease in South Carolina. *Arch Dermatol* 1983; 119: 650–654.
4. Nixon R, Frowen K, Moyle M. Occupational dermatoses. *Aust Fam Physician* 2005; 34: 327–333.
5. Lodi A, Chiarelli G, Mancini L L et al. Allergic contact dermatitis from a rubber bracelet. *Contact Dermatitis* 1996; 34: 146.
6. Rycroft R J G, Menne T, Frosch P J et al. *Textbook of Contact Dermatitis*, 3rd edition. Heidelberg: Springer Verlag, 2001.
7. Dooms-Goossens A, Degreef H, de Veylder H et al. Unusual sensitization to black rubber. *Contact Dermatitis* 1987; 17: 47–48.
8. Kaniwa M, Isama K, Nakamura A et al. Identification of causative chemicals of allergic contact dermatitis using a combination of patch testing in patients and chemical analysis. Application to cases from rubber gloves. *Contact Dermatitis* 1994; 31: 65–71.
9. Vaswani S K, Collins D D, Pass C J. Severe allergic contact eyelid dermatitis caused by swimming goggles. *Ann Allergy Asthma Immunol* 2003; 90: 672–673.
10. Weinberger L N, Seraly M P, Zirwas M J. Palmar dermatitis due to a rubber escalator railing. *Contact Dermatitis* 2006; 54: 59–60.
11. Ho V C, Mitchell J C. Allergic contact dermatitis from rubber boots. *Contact Dermatitis* 1985; 12: 110–111.
12. von Hintzenstern J, Heese A, Koch H U et al. Frequency, spectrum and occupational relevance of type IV allergies to rubber chemicals. *Contact Dermatitis* 1991; 24: 244–252.

13. Krob H A, Fleischer A B Jr, D'Agostino R Jr et al. Prevalence and relevance of contact dermatitis allergens: a meta-analysis of 15 years of published T.R.U.E. test data. *J Am Acad Dermatol* 2004; 51: 349–353.
14. Menne T, White I R, Bruynzeel D P et al. Patch test reactivity to the PPD-black-rubber-mix (industrial rubber chemicals) and individual ingredients. *Contact Dermatitis* 1992; 26: 354.
15. Hansson C. Allergic contact dermatitis from N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine and from compounds in polymerized 2,2,4-trimethyl-1,2-dihydroquinoline. *Contact Dermatitis* 1994; 30: 114–115.
16. Fisher A A. Allergic reactions to nonrubber products by testing with rubber mixes. Part III: The black rubber mix. *Cutis* 1995; 56: 253–254.
17. Dotterud L K, Falk E S. Contact allergy in relation to hand eczema and atopic diseases in north Norwegian schoolchildren. *Acta Paediatr* 1995; 84: 402–406.
18. Lammintausta K, Kalimo K, Fagerlund V L. Patch test reactions in atopic patients. *Contact Dermatitis* 1992; 26: 234–240.
19. Brasch J, Geier J. Patch test results in schoolchildren. Results from the Information Network of Departments of Dermatology (IVDK) and the German Contact Dermatitis Research Group (DKG). *Contact Dermatitis* 1997; 37: 286–293.

Address:
D. I. M. Kuijpers, MD
Department of Dermatology
University Hospital Maastricht
P. Debijelaan 25
PO Box 5800
6202 AZ Maastricht
the Netherlands
Tel: +31 43 3875292
Fax: +31 43 3877293
e-mail: dku@sder.azm.nl