

Occupational Allergic Contact Dermatitis from Antioxidant Amines in a Dental Technician

Luis Conde-Salazar, Ruud Valks, Carmen García Acebes, and Josep Bertó

We describe an 18-year-old dental technician who presented with dry hyperkeratotic lesions on his left palm that were limited to an area that was in contact with a container in which he had prepared the molds for a dental prosthesis. On patch testing, he had a positive reaction to black rubber mix and its components N-cyclohexyl-N'-phenyl-4-phenylenediamine, N,N'-diphenyl-4-phenylenediamine, and N-isopropyl-N'-phenyl-4-phenylenediamine, as well as to a piece of the rubber container. Thin-layer chromatography (TLC) of a piece of the rubber container confirmed the presence of the para-phenylenediamine mix. Results of patch-testing with TLC were positive after 48 and 96 hours. The lesions resolved when the patient stopped using the container. The patient was diagnosed with occupational allergic contact dermatitis. We also review the dermatoses caused by antioxidant amines.

THE INCIDENCE OF SENSITIZATION TO RUBBER has increased over the last years as a result of major industrialization and the greater use of rubber products.¹ Automation and the mechanization of the rubber industry have decreased the cases of sensitization to rubber among the workers who manufacture it, but major use of rubber in gloves and boots has resulted in a major frequency of sensitization to rubber in users. In a study performed in this department, sensitization to black rubber was seen most frequently in construction workers, who use gloves as a protective measure.² The dermatitis was most frequently seen in persons between the ages of 20 and 50 years, with a predominance in men, probably because men usually are predominant in the occupations that are associated with allergic contact dermatitis to black rubber.¹⁻⁴

In the manufacturing of rubber, numerous additives are used to improve elasticity and prevent rapid degradation. The main additives are (1) accelerators of vulcanization and (2) antioxidants (or antidegradants), both of which may cause cutaneous problems. The natural components of rubber rarely induce type IV hypersensitivity.^{1,3,4}

However, latex may produce immediate type I hypersensitivity reactions.

Rubber intolerance may produce various clinical manifestations.⁵ Allergic and irritant dermatitides are most common. Allergic reaction to the amine antioxidants often presents as a typical hyperkeratotic dermatitis simulating psoriasis over the palms and soles. More rarely seen are purpura,⁶ pigment alterations, and the syndrome of purpura, petechiae, pruritus, and sensitization to N-isopropyl-N'-phenyl-4-phenylenediamine (PPPP syndrome).^{7,8} The site of involvement is mainly the hands as they are the areas of major contact. The lesions resolve rapidly with avoidance of the causative allergen, which may be difficult to achieve as some allergens may be found not only in industrial products but also in medicines, food, and domestic products.¹ Among the additives in these products, the antioxidants or antidegradants are of great importance because they stabilize the polymer, inhibiting tears and preventing brittleness provoked by oxidation over the years.

The most important antidegradants are the amine antioxidants, which are derivatives of para-phenylenediamine (PPD), greatly used in industry (nowadays), and which have a very high capacity of sensitization. Together with the thiuram group (accelerators of the vulcanization of rubber), they are substances of major interest to the dermatologist. The principal uses of the amine antioxidants are indicated in Table 1. The most important amine antioxidant derivatives are N-isopropyl-N'-phenyl-4-phenylenediamine (IPPD), N-cyclohexyl-N'-phenyl-4-phenylenediamine (CPPD), and N,N'-diphenyl-4-phenylenediamine (DPPD).

From the Servicio de Dermatología Laboral, Escuela Nacional de Medicina del Trabajo, Instituto de Salud Carlos III, Madrid, Spain.

Address reprint requests to Luis Conde-Salazar Gómez, MD, PhD, Servicio de Dermatología Laboral, Escuela Nacional de Medicina del Trabajo, Instituto de Salud Carlos III, Cuidad Universitario, Pabellón 8, 28040 Madrid, Spain; E-mail: lconde@isci.es

Table 1. Principal Items and Devices Containing Amine Antioxidants

Car industry products (tires, straps)
Electrical appliances
Cables
Milk machines
Sports shoes, protective boots
Sports utensils (diving suits, goggles, sailboards)
Protective masks
Goggles
Cases for eyeglasses
Hoses
Orthopedic bandages
Diving equipment
Cutting fluids
Rubber fingers
Escalator handrails
Dental containers

These are patch-tested together as PPD mix, in which CPPD and DPPD are diluted to 0.25% and IPPD diluted to 0.1% in petrolatum. They are also tested separately, CPPD and DPPD at 1% and IPPD at 0.1% in petrolatum. Their similar chemical structures and the coincidence of various positive patch-test reactions suggest the possibility of cross-reactions among them.¹⁻⁴ However, this coincidence of various positive reactions may be secondary to concomitant or multiple sensitizations as the amine antioxidants are found in numerous products and as the same product may contain various amines.²

Kaniwa and colleagues believe that patch testing and chemical analysis should be combined to confirm the relevance of positive patch-test reactions and to discover new allergens.⁹ Accordingly, Bruze and colleagues suggested performing patch tests with the components revealed by thin-layer chromatography (TLC) in order to confirm probable sensitization.¹⁰

Case Report

An 18-year-old dental technician had a 3-week history of itchy erythema on the palm and fingers of his left hand, with development of hyperkeratotic lesions and fissures (Fig 1). He also reported occasional blisters. He had received treatment with corticosteroid creams, which improved the lesions. The patient had been making dental prostheses for 2 years. Four weeks before the development of the lesions, he had begun to use a black rubber container, in which he prepared the molds for dental prostheses. He used no protective measures during his



Figure 1. Left hand of an 18-year-old dental technician with a 3-week history of itchy erythema on the palm and fingers, showing the development of hyperkeratotic lesions and fissures.

work. On physical examination, well-defined erythematous hyperkeratotic plaques with occasional fissures were observed on the palm and on the palmar and lateral aspects of the third and fourth finger of his left hand. The lesions coincided with the area that had been in contact with the rubber container.

Patch testing was performed with the European Standard series, a dental acrylates series, a rubber additives series, and an epoxy series (all from Chemotechnique, Malmö, Sweden). After 48 and 96 hours, positive reactions to PPD mix, PTD, CPPD, DPPD, and IPPD were observed.

The patient brought us the container (Mestra) he used in his work and showed us the way he used it (Fig 2).



Figure 2. Illustration of the black rubber container and its use by the patient.



Figure 3. Result of a patch test with a piece of the container.

Patch-testing with a piece of the container, with readings at 48 and 96 hours, yielded a ++ reaction (Fig 3). Control patch tests using a piece of the container gave negative results in 20 volunteers. Because we could not obtain the composition of the container, we sent a piece of it to the occupational dermatologic laboratory of Prof. Magnus Bruze in Malmö, Sweden, where TLC was performed. TLC revealed that the container contained IPPD. Subsequently, patch tests with thin-layer chromatograms were carried out (the chromatograms, made with 50 μ L and 100 μ L of rubber extract, were also developed at the laboratory of Prof. Bruze).¹⁰ Positive results (+++) at 48 and 96 hours were shown by both chromatograms (Fig 4).

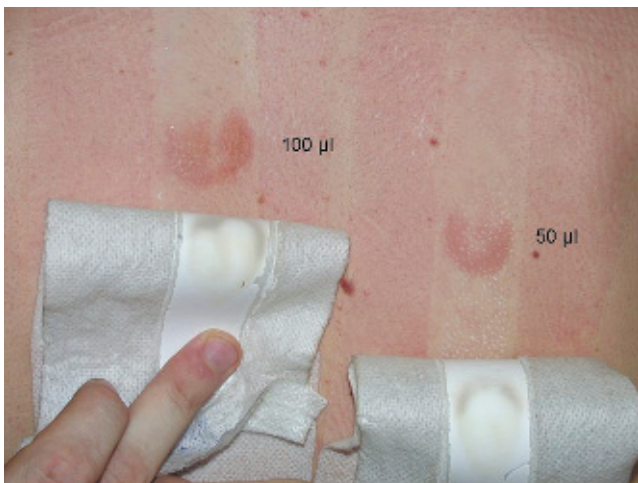


Figure 4. Positive results at 96 hours of a patch test using thin-layer chromatograms made with 100 μ L and 50 μ L of rubber extract.

During the 15 days of patch testing, in which the patient did not work, all lesions resolved almost completely. A diagnosis of occupational allergic contact dermatitis from the rubber material that he used in his work was made. We recommended that he substitute a plastic container for the rubber one and that he avoid the allergens to which he was sensitized, both in his occupational life and in his private life.

Discussion

Lesions on the hands and especially on the palms may be a diagnostic challenge for the dermatologist. Dermatologic conditions such as eczema, psoriasis, lichen planus, and keratoderma can all give very similar clinical pictures, and without lesions at other sites of the body, a correct diagnosis may sometimes be impossible to make. However, well-directed and well-performed patch testing may help establish a correct diagnosis in many cases.

Allergic contact dermatitis from rubber components, such as accelerators of vulcanization and such as antioxidants, may give various clinical manifestations. A special form of such dermatitis, called “hands and feet of the black rubber,” is produced by amine antioxidants (IPPD and derivatives) and presents as dry hyperkeratotic lesions on the palms and soles that resolve spontaneously with avoidance of the causative allergens. Differential diagnosis should include psoriasis and keratoderma. Clinical recognition and well-performed patch testing with the European Standard series and with a rubber additives series usually establish the definitive diagnosis.

Determining the exact composition of a rubber product is difficult; in many cases, the exact composition is unknown, or the industry gives only global information (eg, that the rubber product contains antioxidants) without further details. In those cases, we usually can confirm the diagnosis of allergic contact dermatitis from rubber by performing a patch test with a piece of the rubber product humidified with water or alcohol. TLC or gas chromatography may reveal the various antioxidant components in the rubber.¹¹ Accordingly, some authors suggest performing patch tests with the extracts obtained by chromatography in order to find the allergen responsible for the lesions.¹⁰

We have described a new case of allergic contact dermatitis from the amine antioxidants in black rubber, indicated by (1) positive patch-test reactions to PPD mix and its components IPPD, DPPD, and CPPD; (2) a positive reaction to IPPD in the chemical analysis of the black rubber container that our patient used in his work;

and (3) a positive patch-test reaction to a black rubber thin-layer chromatogram. We would like to emphasize the feasibility and usefulness of patch-testing with chromatography plates in selected cases.

Acknowledgment

We wish to thank Drs. Magnus Bruze and Birgitta Gruvberger, Malmö, Sweden, for preparing the thin-layer chromatography for patch testing.

References

1. Conde-Salazar L. Dermatitis por gomas y sus componentes. In: Conde-Salazar L, Ancona Alayon A, editors. *Dermatología profesional*. Madrid: Grupo Aula Medica SL; 2004. p. 87–106.
2. Conde-Salazar L, Guimaraens D, Romero LV, Harto A. Sensibilidad a aminas antioxidantes. *Actas Dermosifiliogr* 1984;1-2:23–36.
3. Conde-Salazar L, Del Río E, Guimaraens D, González Domingo A. Type IV allergy to rubber additives: a 10 year study of 686 cases. *J Am Acad Dermatol* 1993;29:176–80.
4. Conde-Salazar L, Guimaraens D, González Domingo MA. Dermatitis de contacto por gomas. *Piel* 1991;6:160–72.
5. Conde-Salazar L. Rubber dermatitis. Clinical forms. *Dermatol Clin* 1990;8:49–55.
6. Roed-Petersen J, Clemmensen OJ, Menné T, Larsen E. Purpuric contact dermatitis from black rubber chemicals. *Contact Dermatitis* 1988;18:166–8.
7. Fisher AA. Allergic petechial and purpuric rubber dermatitis: the PPPP syndrome. *Cutis* 1974;14:25–7.
8. Romaguera C, Grimalt F. PPPP syndrome. *Contact Dermatitis* 1977;3:102–3.
9. Kaniwa MA, Isama K, Kantoh H, et al. Identification of causative chemicals of allergic contact dermatitis using a combination of patch testing in patients and chemical analysis. *Contact Dermatitis* 1994;30:20–5.
10. Bruze M, Frick M, Persson L. Patch testing with thin-layer chromatograms. *Contact Dermatitis* 2003;48:278–9.
11. Harto A, Conde-Salazar L, Parra Bravo L. Identificación de las aminas antioxidantes en *Dermatología Laboral*. *Med Segur Trab* 1981;115:111–5.