



**Figure 2** Immunoblotting of samples illustrated in Fig. 1 with the serum of the allergic subject.

In our study, we demonstrated a sensitisation to  $\beta$ -casein from buffalo's, ewe's and goat's milk without any reactivity to cow's milk proteins.

So far very few clinical studies have been published on the relationship between buffalo and cow's milk allergy, probably because of a general awareness of the high homology between these two animal species and the usual avoidance of buffalo's milk derivatives (such as mozzarella) by cow's milk allergic subjects. Buffalo's milk allergy may be isolated, without any other Bovidae mammalian allergy,<sup>2</sup> but this case report suggests that there is the possibility of an associated goat-ewe-buffalo's milk allergy without cow's milk allergy, and it helps in order to give the right advice on milk avoidance.

## Ethical disclosures

**Protection of human and animal subjects.** We declare that no experiments were performed on humans or animals for this investigation.

**Confidentiality of data.** We declare that we have followed the protocols of our work centre on the publication of patient data and that the patient included in the study has received sufficient information and has given his informed consent in writing to participate in that study.

**Right to privacy and informed consent.** We have obtained the informed consent of the patient's relatives in the study. We for correspondence are in possession of this document.

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## Polysensitisation to rubber additives and dyes in shoes and clothes

To the Editor,

Many allergens are involved in contact dermatitis of clothing and footwear. Shoes include rubbers, dyes, glues and leather, and a wide range of components, which depend on the epidemiological and geographical situation of the individual.<sup>1–3</sup> In textiles, the azo dyes are mainly responsible for acute clinical reactions requiring medical intervention,<sup>3</sup> while synthetic resins mainly cause chronic reactions.<sup>4</sup> Other substances used in their manufacture, such as vulcanisation

accelerators, elastic, and decorative objects occasionally cause allergy.<sup>1</sup>

A 56-year-old Caucasian male patient, bus driver, admitted after widespread eczema, predominantly acral, which was confirmed on histological examination. He received outpatient treatment with betamethasone, and subsequently he was readmitted for microbial eczema of the feet that spread through the trunk and the extensor surface of the upper and lower limbs. He was treated with prednisolone 20 mg and flucloxacillin, as well as washing with potassium permanganate. Mycological examination of scales of the feet was negative. In his profession, he wore shoes with black rubber soles and a dark blue suit of synthetic fabric which we

later discovered was part of his uniform. He denied personal and family history of atopy.

The patch test was performed with the basic adopted by GPEDC (Grupo Português de Estudo das Dermite de Contacto) and shoes series (both from Chemotechnique diagnostics 2009 (Malmö, Sweden)).

Analysing the results obtained, IPPD is an anti-ozonant for the vulcanisation of black rubber and, also related with shoes, 1,3-diphenylguanidine and n-dodecyl mercaptan are vulcanisation accelerators of natural and synthetic rubber, respectively. The Disperses Blue 106 and D. Orange 1 are clothing dyes, as well as D. Orange 3, D. Yellow 3, D. Red 1, D. Blue 3, also commonly used in socks, and Acid Yellow 36 which is regularly used in shoes. There was no reaction to PPD.

In order to better understand the patient's reaction and to evaluate the use of the uniform (dark blue synthetic fabric) without any other material composition we carried out a patch test series of textile dyes (textile dyes and resins) using fragments of the individual clothes (Table 1)

N-isopropyl-N'-phenyl-p-phenylenediamine (IPPD) is an anti-ozonant of rubber vulcanisation and the major allergen of black rubber, and was assumed to be responsible for the onset of the feet eczema, once the patient was wearing shoes with black rubber soles.

1,3-Diphenylguanidine is also a vulcanisation accelerator for natural rubber as well as n-dodecyl mercaptan for synthetic rubber, since both components exist in the shoes, it could explain a concomitant sensitisation process due to their different chemical structures. 1,3-Diphenylguanidine can be an irritant substance in the patch tests and may give false positive reactions. In our case the result was a delayed reaction to this component as seen in the increase response comparing the reading at D2 and D4.

**Table 1** Readings at 48 and 96 h of the following series: basic, textile, fragments of the individual clothes and shoes.

	D2	D4
<i>Basic series</i>		
IPPD 0.1% pet	+++	+++
Disperse Blue 106 (1% pet)	++	++
PPD 1% pet	—	—
Disperse Orange 1 (1% pet)	+++	+++
<i>Shoe series</i>		
D. Orange 3 (1% pet)	++	+++
D. Yellow 3 (1% pet)	++	+++
D. Red 1 (1% pet)	++	+++
D. Blue 3 3 (1% pet)	?	+++
Diphenylguanidine (1% pet)	++	+++
Acid Yellow 36 (1% pet)	+++	+++
Dodecyl mercaptan (0.1% pet)	++	+++
<i>Textile dyes and resins</i>		
4-Aminoazobenzene (0.25% pet)	+++	+++
Disperse blue-124 (1% pet)	++	+++
Disperse yellow-9 (1% pet)	—	+
Disperse black-1 (1% pet)	?	++
Fragment of blue suit (as is)	—	—
Fragment of blue socks(as is)	—	—

IPPD has structural similarity to PPD and may therefore cross-react with it,<sup>5</sup> and in this case it is not proved. Allergy to textile dyes can be caused by the allergen transfer to the skin or by the formation of metabolites after epidermal penetration.<sup>6,7</sup> The final colour is often obtained from the combination of several dyes. The colour of the culprit dye often bears no relationship to the colour of the offending garment. Thus, a blue suit caused dermatitis from a disperse yellow dye used as one component of the final blue colour. The dyes are classified according to their applications. The main allergenic dyes are the dispersed ones, and they come from the azoic (azo) anthraquinone and nitroarylamine (nitro) chemical classes.<sup>6</sup>

The dispersed azo compounds are only partially soluble in water and they are used for dyeing synthetic fibres such as polyesters, acrylics, acetates and sometimes the nylon socks. They are never used in natural fibres.<sup>7</sup> They are characterised by a double bond N=N. This bond has the distinction that in vivo it can be broken down into two amines, which can then be metabolised into haptens.

The disperse yellow-3, disperse orange-1 and disperse red-1, and also disperse blue 106 and 124 are azo dyes. Disperse orange 3 is a dye used in some socks, 66% patients sensitised to this component also react to the PPD, and this can happen by the metabolic conversion of textile dyes in the skin to PPD.<sup>1</sup> They also react to solvent yellow 1 which contains 4-aminoazobenzene and p-dimethyl-4-aminoazobenzene. Azo dyes are characterised by R1—N=N—R2 chemical structures. The rupture of the azoic dye bond is interpreted as a concomitant reaction and not like a cross-reaction, although the allergen formed is the same in both cases.<sup>8,9</sup>

In this patient, the possibility of concomitant reaction or cross-reactivity with disperse dyes has facilitated sensitisation to azo and anthraquinones, whose structures contain a core metabolised benzene which can form PPD.<sup>10</sup> Was thought that dye nitroarylamine (nitro) is a co-sensitisation because it is a different one of the chemical classes of the disperse dyes.<sup>6</sup>

The patient is recommended to avoid wearing clothes of synthetic fibres in direct contact with the skin and especially for dark colours, and with black rubber shoes also.

## Ethical disclosures

**Patients' data protection.** Confidentiality of Data. The authors declare that they have followed the protocols of their work centre on the publication of patient data and that all the patients included in the study have received sufficient information and have given their informed consent in writing to participate in that study.

**Right to privacy and informed consent.** Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects mentioned in the article. The author for correspondence is in possession of this document.

**Protection of human subjects and animals in research.** Protection of human and animal subjects. The authors

declare that the procedures followed were in accordance with the regulations of the responsible Clinical Research Ethics Committee and in accordance with those of the World Medical Association and the Helsinki Declaration.

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## Allergic hypersensitivity to Deflazacort

To the Editor:

Corticosteroids are potent anti-inflammatories and immunomodulators used in the treatment of various inflammatory and allergic reactions that can cause delayed and immediate hypersensitivity, often misdiagnosed because of atypical clinical presentation.<sup>1</sup> There are four main groups (A, B, C and D with subgroups D1 and D2) defined by their chemical properties and depending on their molecular structure. Skin metabolism plays an important role in the allergenicity of corticosteroids and also influences the profile of cross-reactions.<sup>2–3</sup>

A 31-year-old-Caucasian female, lawyer, was assisted in the emergency room, after an exuberant swelling of her eyelid caused by an insect bite. She was treated initially with intravenous hydrocortisone and after discharge, with deflazacort (6 mg per day), clarithromycin and topical hydrocortisone. The patient returned to the emergency room 24 h later, for a widespread rash showing some individualised erythematous-pink plaques with circinate limits and pustules, interpreted as an urticarial reaction or as an acute exanthematous pustulosis.

She denied personal or family history of atopy, but reported an episode of acute dermatitis of the face caused by topical anti-acne cream, ten years before. Hypersensitivity to neomycin, tixocortol pivalate, Kathon CG, thimerosal, nickel, cobalt and benzoyl peroxide had been demonstrated in patch test performed that time.

The following immunoallergy tests were carried out: prick tests and intradermal tests with deflazacort 6 mg, hydrocortisone and clarithromycin in increasing

dilutions. In addition, patch tests were performed with the basic series adopted by (PCDG), a corticosteroid series (including: dipropionate, betamethasone valerate, dexamethasone, triamcinolone, clobetasol, prednicarbat, mometasone, hydrocortisone and tixocortol pivalate), her own drugs and the other drugs already tested in immunoallergy.

Prick tests and intradermal tests: read for 20 min – negative. (immunoallergy). The first positive results were noted (by the patient) after 12 h: hydrocortisone and deflazacort 6 mg (Fig. 1, Table 1).

Hypersensitivity was shown to tixocortol pivalate (a Group A substance), as well as to hydrocortisone (Group A)



Figure 1 Reading of intradermal tests at 48 h.