

**Contact dermatitis to
4-amino-2-hydroxytoluene
in hair dye**

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p-Phenylenediamine (PPD) was first mass marketed by French chemist Eugene Schueller at the beginning of the 20th century through his French Harmless Hair Dye Company (1) – which eventually became L'Oreal. Over the past 110 years, numerous case reports have shown that PPD is anything other than 'harmless' (2), with PPD now used as the main component of the European baseline patch test series to detect hair dye allergy.

Case Report

We report the case of a 47-year-old female jeweller who presented with a 3-week history of a scaly, erythematous scalp, which began the day after the application of a brown semi-permanent hair dye. She had used a different hair dye previously without problems. Patch testing was performed to the British Contact Dermatitis Society baseline series and metal, facial, and hairdressing series (IQ ultra[®] patch test chambers, allergens from Chemotechnique Diagnostics[®] AB, Malmo, Sweden). One additional component of the hair dye that fell outside of these series was supplied by the hair dye manufacturer. Positive reactions are outlined in Table 1. Of these, 4-amino-2-hydroxytoluene (CAS no. 2835-95-2, common synonyms 5-amino-*o*-cresol and 4-amino-2-hydroxy-1-methylbenzene) has not been reported before in the literature as a contact allergen (3, 4).

Comment

In 2004, Søstet et al. (5) reviewed the 229 most common substances found in hair dyes in the EU. They were able to propose a list of ingredients for patch testing of patients with suspected hair dye dermatitis based on quantitative structure-activity relationships (QSARs), which may predict the likelihood of skin sensitization potential through the assessment of

Table 1. Patch test results

Hair dye chemicals	% vehicle	D2	D4
PPD	1% pet.	++	+++
<i>p</i> -Toluenediamine sulfate	1% pet.	++	+++
4-Amino-2-hydroxytoluene (Procter & Gamble, Galashiels, UK)	1% pet.	++	++
<i>o</i> -Nitro PPD	1% pet.	+	+
3-Aminophenol	1% pet.	+	+
4-Aminophenol	1% pet.	+	+

PPD, phenylenediamine.

the molecular structure of each chemical (6), and raw tonnage data of the amounts of each constituent used in the EU annually. In conjunction with this, a literature review of previously documented hair dye contact allergies was undertaken.

4-Amino-2-hydroxytoluene is a 'colour coupler' used in oxidative dye compositions to aid a deep red colour. It is one of the most commonly used chemicals by total weight and is rated as a moderate sensitizer by the QSAR method (3), which led to Søstet et al.'s suggestion of it being included in patch tests for hair dye allergy. It is interesting that our patient reacted to three chemicals from a similar 'cluster', based on physiochemical properties and reactivity, used in the Søstet et al. paper (5). This adds weight to their assertion that there is a plausible similarity in sensitization capacity within these groupings [this is in no way assured, however, as shown by Winhoven et al. (7), who described isolated *p*-toluenediamine contact allergy in patients who showed no reaction to the chemically similar PPD].

In the case of 4-amino-2-hydroxytoluene, as yet unpublished anecdotal evidence suggests that positive reactions to this chemical are always accompanied by reactions to PPD. This cross-reactivity would make a positive result to 4-amino-2-hydroxytoluene less clinically relevant. Therefore, in response to the suggestions by Søstet et al. (5) that any screening hairdressing series should aim to cover a full spectrum of physiochemical properties, we feel that 4-amino-2-hydroxytoluene should not be included in any form of routine testing until a larger case

series of positive reactions to it can be analysed.

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