Ethylenediamine allergy – a historical problem?

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Ethylenediamines are a structural class of antihistamines developed in the 1940s, which have other useful functions. Ethylenediamine dihydrochloride (EDA) is currently a constituent of parenteral aminophylline, insecticides, lubricants, herbicides, metal polishes, detergents, floor polish removers, waxes, rubbers, dyes, freezing/cooling solutions, epoxy curing agents and bleach accelerators (Dittmar D, Politiek KM, Coenraads P-J et al. Contact Dermatitis 2017; 76: 310-12). EDA is no longer present in any prescribed cream in the U.K.

The first case report of cutaneous allergy to EDA was in 1958 (Tas J, Weissberg D. Allergy to aminophylline. Acta Allergol. 1958; 12: 39-42). From 1968, routine patch testing to EDA in baseline series was recommended due to the high frequency of sensitisation. In recent years allergy to EDA has declined. It was removed from the European Baseline Series in 1995. Tri-Adcortyl® cream (containing EDA as a preservative, emulsifier and stabiliser), the most common source of allergy to EDA in the U.K., was discontinued in 2009. The resulting decrease in the frequency of

positive patch tests led EDA to be removed from the BSCA baseline series in March 2018.

We wished to assess the current prevalence of sensitisation to EDA, and its relevance. We performed a retrospective audit using data from 12 patch test centres in the U.K., examining the rate of sensitisation to EDA in consecutively tested patients between 2013 and 2018 and the relevance of any positive patch tests, where known. 20,456 consecutive patients were tested and 127 (0.62%) had a positive patch test to EDA. Demographics were available for 112 of these patients. Two-thirds (70%) were female (n=78); the mean age was 59.4 years (median 60). 41 of the 127 patients sensitised to EDA (32%) had positive tests deemed to be of current (19) or past (22) relevance. Tri-adcortyl® was the source of sensitisation in 16 of 22 cases with past relevance. Other sources of exposure included rubber, aminophylline and topical nystatin. In some cases, sensitisation was thought to reflect exposure to cross-reacting oral antihistamines, including hydroxyzine. Only one case was thought to be occupational.

EDA is now a rare sensitizer, and in most patients with positive patch tests relevance cannot be determined. In the last decade, reported cases have largely been due to occupational exposure**.** We suggest that EDA be reserved for occasional testing in selected patients with a history of relevant occupational exposure, or in those with severe dermatitis after exposure to intravenous aminophylline.