

patch was applied for 1 day and reactions were scored 1 and 3 days after patch removal. In the photoallergy study, the test substance was applied to 2 different locations 2×/week for 3 weeks (5). 10 min after patch removal, 1 site was irradiated with UV light (16–20 J/cm²) while the other site acted as control. The induction period was followed by a 2-week rest period prior to application of the 1-day challenge patch. Patch sites were again irradiated and reactions were scored at 1 h and 1, 2 and 3 days post-irradiation. These studies identified 1 individual from each study with reactions suggestive of sensitization induction. The skin reaction observed in the individual from the photoallergy study occurred at both the irradiated and non-irradiated sites, indicating that irradiation was not needed for elicitation.

A 3rd study was conducted approximately 30 months later to reaffirm the sensitivity of these 2 individuals and to determine a no observable effect level (NOEL). Panelists were exposed to ascending concentrations of TBHQ (0.0003–0.02%) in 0.2 ml of pet. until a positive allergic response was elicited. Patches were left on for 2 days and sites were scored at 0.5 h and 2 days post removal. Both individuals exhibited reactions indicative of contact sensitization at concentrations of 0.010% and 0.020%. The NOEL for eliciting a reaction to TBHQ was determined to be 0.0050% (50 ppm).

Discussion

Monotertiary butyl hydroquinone has safely been used in the food and cosmetics industries for many years. There are isolated case reports of individuals exhibiting various dermatitis reactions who have tested positive to TBHQ in challenge patch tests (6–8). A lack of photosensitization in humans is in agreement with negative results seen in laboratory animal photoallergy studies

(3). Results of other guinea pig sensitization studies indicate that TBHQ is a weak sensitizer (2, 3). The studies above, along with those in laboratory animals and case reports, suggest that the potential for TBHQ to induce sensitization in humans is low when used as intended. However, these data substantiate that its use in cosmetics should be at the minimal level needed to achieve its intended effect and should not exceed the CIR recommended maximum of 0.1%. The small size of the data set, and our general information about human variation in sensitivity to contact allergens, mean that these numbers should be considered tentative approximations until more information becomes available.

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Photosensitivity due to doxycycline hydrochloride with an unusual flare

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A 42-year-old man was seen in July 1996 with scaly erythema and vesicles on the face, neck (Fig. 1), arms, and dorsa of the hands and feet that had started 3 days earlier. He had no past history of photosensitivity. He had been taking doxycycline hydrochloride (Vibramycin®, Pfizer Pharmaceut. Inc., Tokyo) 100 mg b. d., flavin adenine dinucleotide sodium 10 mg t. d. s., and pyridoxal phosphate 20 mg t. d. s. orally because of acne vulgaris for a week. There were no abnormal findings on hematological examination, blood chemistry, or uri-

nalysis, including porphyrins of peripheral erythrocytes and urine. Histological findings of erythema on the nape of the neck demonstrated parakeratosis, hydropic degeneration of the basal layer, and perivascular edema and lymphohistiocytic infiltration. Sunburn cells were not seen.

We performed a screening phototest, as described before (1), with a Dermalay Model M-DMR-1 (Eisai Co. Ltd.) as a light source (2, 3). UVB-MED for this patient was normal (50 mJ/cm²), while 11.25 J/cm² of UVA-ir-



Fig. 1. Scaly erythema on the neck.



Fig. 2. A flare on the neck after taking doxycycline hydrochloride.

radiation, which was less than 13.5 J/cm^2 , produced erythema on the irradiated area at 1 day after the irradiation. A screening phototest was performed again 2 weeks after the patient stopped taking the 3 drugs. Irradiation of 13.5 J/cm^2 for UVA elicited no response, suggesting that photosensitivity to UVA of the patient had become normal. Patch and photopatch tests were made with doxycycline hydrochloride, minocycline hydrochloride, flavin adenine dinucleotide sodium, and pyridoxal phosphate (10 and 1% pet.). Only 10% pet. of doxycycline hydrochloride with UVA-irradiation (4.5 J/cm^2) on photopatch testing showed small papules on erythema 1 day after irradiation. Patch and photopatch tests with doxycycline hydrochloride, flavin adenine dinucleotide sodium, and pyridoxal phosphate in 5 normal subjects showed no erythema or papular response 2 days after application or 1 day after irradiation.

1 h after the patient took 100 mg of doxycycline hydrochloride for oral photochallenge testing, erythema was seen with itching and burning sensation only on the exact areas that had been previously involved (Fig. 2). The photochallenge test was discontinued because of this unexpected flare.

Discussion

Doxycycline is a potent photosensitizer and has been reported as causing a high incidence of phototoxic reactions (4). In the present case, however, a flare was provoked by oral administration of the drug alone, which suggests a photoallergic reaction rather than a phototoxic one. A photoallergic reaction usually occurs at intervals as a result of drug plus light, but sometimes due to either drug or light alone (5), whereas phototoxic reactions occur exclusively on skin areas exposed to a combination of drug and light (5). Therefore, we consider that our patient may be a rare case of photoallergy due to doxycycline.

It is well-known that flares are occasionally seen in photopatch testing for photoallergy (6). Although the mechanism of flares remains unresolved, photoantigen formed at the site of testing could play an important rôle. 4 possibilities have been proposed for the formation of photoantigen in skin (5): (i) the hapten formed by irradiation combines with a skin protein to form an antigen; (ii) the hapten combines with the protein changed by light to form an antigen; (iii) the hapten formed by irradiation combines with the protein changed by light, thus forming an antigen; (iv) the hapten and light catalyze a chemical reaction on the protein which leads to an autoantigen. In the present case, the 2nd possibility is most likely, since simultaneous exposure of the drug and light was not necessary. Carrier protein, previously formed by light, may still be present in this patient's skin and may be combined with the drug or its metabolite to form photoantigen and cause a flare.

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