

Budesonide Allergic Contact Dermatitis “by Proxy”?

To the Editor:

Inhaled corticosteroids (CS), widely used to treat allergic and inflammatory respiratory diseases, can sensitize the patient or the cohabiting/caregivers. Allergic contact dermatitis (ACD) seems to occur more frequently in the second group representing 5% of all 315 CS allergic patients versus only 4% of personal users.¹ One explanation for this could be induction of oral/nasal tolerance in patients who use inhaled CS, decreasing the possibility of sensitization.^{1,2}

A 32-year-old man presented with a 3-month history of recurrent vesiculobullous lesions on the dorsum of his right hand, sometimes extending to the forearm and arm (Fig. 1). Betamethasone dipropionate cream and occasionally oral CS were required for resolution. He mentioned gardening as his hobby; therefore, plant dermatitis or phytophotodermatitis was suspected. Patch testing was performed with the European/Portuguese baseline series, rubbers, and plants series (Chemotechnique Diagnostics, Vellinge, Sweden), with readings on day 2 and day 3 according to the International Contact Dermatitis Research Group recommendations. Positive reactions were observed to fragrance mix I 8% petrolatum (pet) and II 14% pet (++), carba mix 3% pet (+), hydrocortisone-17-butyrate 0.1% pet (++), and budesonide 0.01% pet (++). Further patch testing with fragrance and CS series gave additional positive reactions to alclomethasone dipropionate 1% pet (++) and a methylprednisolone aceponate cream (Advantan cream, Intendis Manufacturing S.p.A., Milano, Italy) (++). Perfume allergy did not correlate with the clinical presentation, and CS reactivity looked nonrelevant, given the rapid response to CS. In addition, the patient denied use of these CS.

Some weeks later, the patient returned to the clinic with another outbreak. With the knowledge of his CS allergy, he questioned the possibility of his contact with budesonide spray (Pulmicort, AstraZeneca AB, Södertälje, Sweden) during asthma treatment for his 2-year-old daughter, who had very recently been diagnosed with asthma. The patient began

avoiding exposure to the budesonide-containing aerosol, and no more episodes of dermatitis have occurred.

Up to 5% of patch-tested patients are reactive to at least 1 CS.³ Budesonide is a nonhalogenated, medium-potency topical CS and the most commonly used molecule in liquid aerosols. In the newest and simplified classification that includes 3 groups of related CSs causing contact allergy, provided by Baeck et al,⁴ budesonide belongs to group 1 and is responsible for most contact allergic reactions to CS (Fig. 2). Nevertheless, reactions are often considered nonrelevant, perhaps because of the fact that allergic dermatitis “by proxy” is undervalued in clinical practice. A recent review collected 15 patients in whom contact allergy to CS, and presumably contact sensitization, occurred because of airborne exposure to steroid-containing aerosols, particularly budesonide, in individuals who were not using CS for their own treatment. These individuals were exposed by delivering patient care in a professional setting (nurses), by cohabiting



FIGURE 1. Acute eczema in the dorsum of the right hand, during 1 of the more severe episodes.

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Group 1	Group 2	Group 3
No C ₁₆ -methyl substitution No halogen substitution in most cases	C16/C17 cis ketal or diol structure No halogen substitution except*	C ₁₆ -methyl substitution Halogen substitution
Budesonide Cortisone acetate Fludrocortisone acetate Fluprednisolone acetate Hydrocortisone Hydrocortisone aceponate Hydrocortisone acetate Hydrocortisone 17-butyrate Hydrocortisone 21-butyrate Hydrocortisone hemisuccinate Isofluprednone acetate Methylprednisolone aceponate Methylprednisolone acetate Methylprednisolone hemisuccinate Prednisolone Prednisolone pivalate Prednisolone succinate Prednisone Tixocortol pivalate Triamcinolone	Amcinonide Desonide* Flunisolide Fluocinolone acetonide Fluocinonide Halcinonide* Triamcinolone acetonide Triamcinolone diacetate Triamcinolone hexacetonid	Alclomethasone dipropionate Beclomethasone dipropionate Betamethasone Betamethasone 17-valerate Betamethasone dipropionate Betamethasone sodium phosphate Clobetasol propionate Clobetasone butyrate Dexamethasone Dexamethasone acetate Dexamethasone sodium phosphate Diflucortolone valerate Diflorasone diacetate Flumethasone pivalate Fluticasone propionate Mometasone furoate

FIGURE 2. New classification of CS’s according to allergenic groups, provided by Baeck et al.⁴ Main molecules in each group.

with regular users of inhaled CS, or by manipulating aerosols in the treatment of young children,¹ as in our case.

Molecular similarity between budesonide and other CS’s, even from other groups, explains cross-reactions observed in many cases, even when patients did not have contact with the CS, as occurred with alclomethasone dipropionate, which is not commercialized in our country. Group 1 molecules are the more likely to cause delayed hypersensitivity reactions, as in

our case, with reactivity to the budesonide, hydrocortisone-17-butyrate, and methylprednisolone aceponate (Fig. 3). In group 3, C16-methyl substitution in the D-ring and halogenation seem to stabilize the CS molecule, therefore protecting them from metabolization and decreasing sensitizing potential.⁵ Nevertheless, alclomethasone dipropionate, a group 3 molecule (Fig. 4), tested positive in our patient. Halogenation of most of group 3 molecules in position C9 may exert an electrical

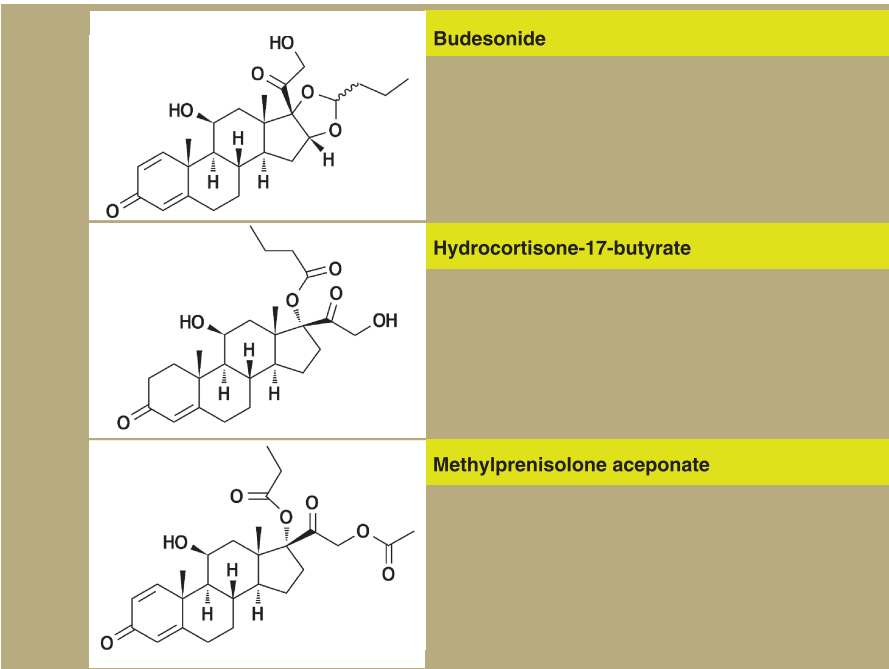


FIGURE 3. Chemical structure of reactive group 1 CS’s: nonmethylated and nonhalogenated molecules.

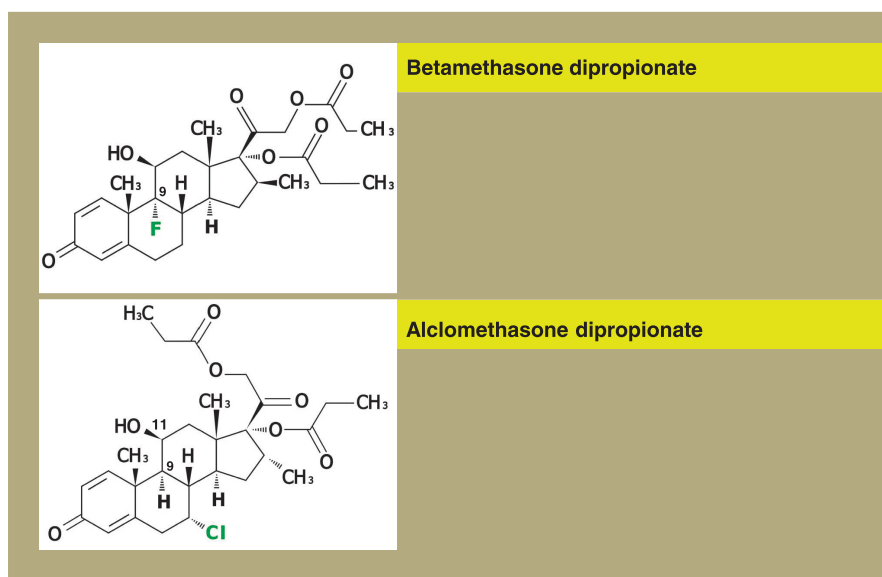


FIGURE 4. Betamethasone dipropionate, tolerated by the patient, and alclomethasone dipropionate, with a ++ test. Both are C16-methylated CS molecules, but C9 halogenation in betamethasone dipropionate may confer more stability to the molecule.

attraction to the carbon C11 and thus stabilize the CS molecule. However, in alclomethasone dipropionate, the halogen (chlorine) is at C6, far from the position C9 considered responsible for molecular stabilization. This could explain allergic reactions observed with alclomethasone dipropionate, despite the classification into the less allergenic group 3.⁵

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Benzoyl Peroxide in Topical Acne Preparations: An Underreported Contact Allergen?

To the Editor:

Although benzoyl peroxide (BPO) is a recognized cause of allergic contact dermatitis (ACD), its sensitization and elicitation from topical acne preparations is rarely reported.¹ We describe 2 cases of facial dermatitis in which patch testing confirmed ACD to BPO that was contained within their acne treatments.

Case 1 is a 20-year-old patient who was admitted to the hospital with acute and progressive facial erythema and edema. There was no personal or family history of atopy, and no other sites were involved. The distribution of the rash was suspicious for a contact dermatitis. Two weeks previously, she had commenced topical treatment with Duac gel (Stiefel, Research Triangle Park, NC) (5% BPO and 1% clindamycin phosphate) for facial acne. Patch testing was performed to our hospital standard battery, face series, relevant parts of the plant series, and her own samples, appropriately applied in Finn chambers on Scanpor tape (Smart Practice, Phoenix, AZ) (Epitest, Finland). The reactions were graded according to the criteria of the International Contact Dermatitis Research Group as follows: ++ to BPO 1% petrolatum (day 4), +++ to Duac 10% in aqueous

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