

Cross-Reactions to Desoximetasone and Mometasone Furoate in a Patient with Multiple Topical Corticosteroid Allergies

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A 60-year-old man developed a bullous contact dermatitis after topical corticosteroid treatment of dermatitis on his lower leg. Subsequent patch testing showed cross-reactions to numerous group B and group D corticosteroids as well as cross-reactions to group C desoximetasone and group D1 mometasone furoate. His patch-test result was negative for the group A corticosteroids hydrocortisone and tixocortol pivalate. We discuss the uncommon finding of cross-reactions to desoximetasone and mometasone furoate.

PATIENTS WITH TOPICAL CORTICOSTEROID ALLERGY frequently present with unresponsiveness to treatment or with exacerbation of their eczema. Patch testing serves not only to confirm an allergy to one or more previously used corticosteroids but also to identify cross-reactions to corticosteroids that were never used but might be prescribed in the future.

Coopman and colleagues noted that corticosteroid cross-reactions often occur within specific groups.¹ Four corticosteroid groups (A, B, C, and D) were defined according to substitution at C16 or C17 on the corticosteroid D ring or substitution at C21 (Fig 1). These include corticosteroids with a C17 or C21 short-chain ester (group A, hydrocortisone type); a C16 C17-cis, -diol, or -ketal chain (group B, triamcinolone acetonide type); a C16 methyl group (group C, betamethasone type); and a C17 and/or C21 long-chain ester (group D, hydrocortisone butyrate type). Group D corticosteroids may be further classified into groups D1 and D2; group D1 corticosteroids contain a C16 methyl group and halogenation of the B ring whereas group D2 corticosteroids lack both of these substitutions. While cross-reactions frequently occur among corticosteroids of the same group,² not all corticosteroids that cross-react in polysensitized patients fit into these four groups.³⁻⁵ In addition, it is difficult to reliably predict whether a specific corticosteroid will be involved in cross-

reactions; patch testing is required in these cases. We report a patient with cross-reactions (on patch testing) to numerous group B, C, and D corticosteroids.

Case Report

A 60-year-old man with a past history of asthma and hay fever was seen at our institution in 1996 in regard to a small area of dermatitis on his lower leg. He was initially treated with betamethasone dipropionate (a group D corticosteroid). The dermatitis persisted, and his topical steroid was changed to fluocinonide (group B), which led to increased erythema, pruritus, and (ultimately) bullae formation. Subsequent administration of hydrocortisone valerate (group D) worsened the erythema. A punch biopsy specimen showed subepidermal bullae with a large number of eosinophils, compatible with a diagnosis of bullous contact dermatitis. Closed patch testing with Finn Chambers (Epitest Ltd Oy, Tuusula, Finland) was performed at that time, and reactions were read and scored according to International Contact Dermatitis Research Group standards.⁶ Reactions to betamethasone-17-valerate, hydrocortisone-17-butyrate, and budesonide were positive (all +++), and reactions to prednisolone and tixocortol pivalate were negative. The initial testing did not include group C corticosteroids. In the ensuing years, the patient avoided group B and D corticosteroids and had no further recurrences of his dermatitis. More recently, the patient returned to the clinic for evaluation of a possible new group A corticosteroid allergy. A new shirt worn by the patient had led to skin irritation on the neck; topical hydrocortisone

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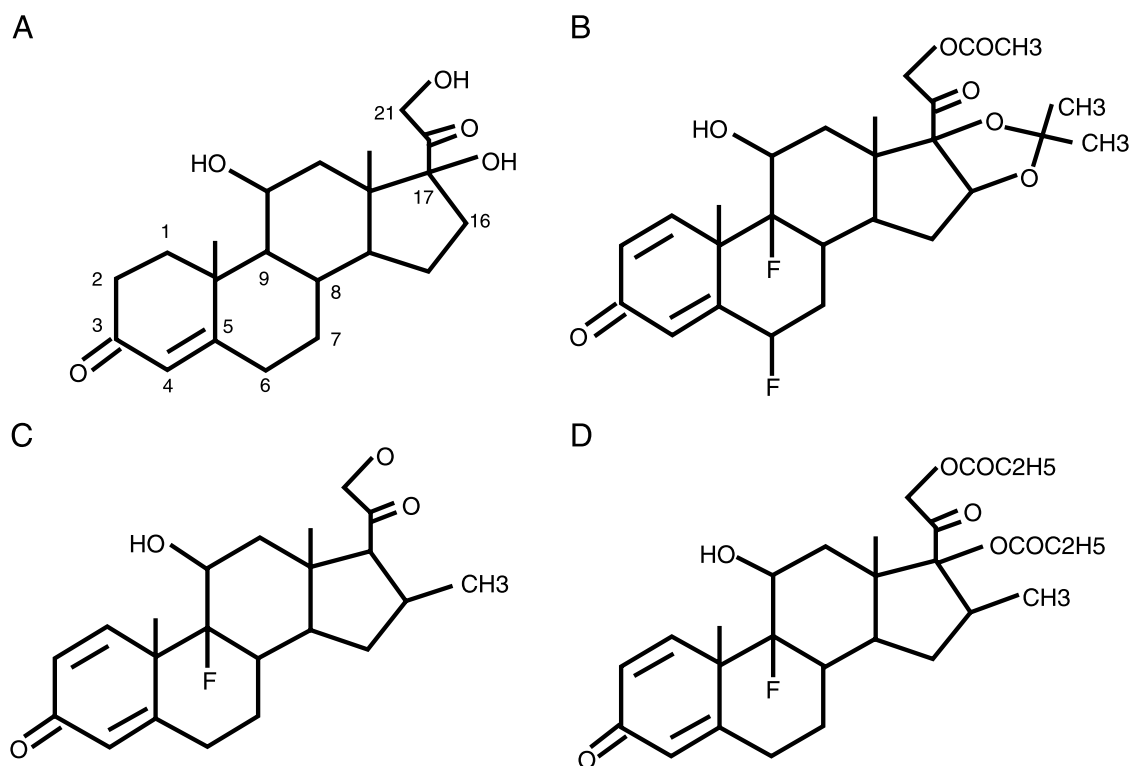


Figure 1. Chemical structures of representative members of corticosteroid groups A–D: A) group A (hydrocortisone) B) group B (fluocinonide) C) group C (desoximetasone) and D) group D (betamethasone dipropionate). Immune recognition sites at C₁₆/C₁₇ and C₆/C₉ are considered important determinants of cross-reaction patterns.

subsequently worsened the irritation. Patch testing was performed with the European Standard tray, a preservative tray, the corticosteroid screening tray, and a wide selection of corticosteroid creams available on the Canadian market (Table 1). Patch-test results were negative for the group A corticosteroids that were tested but confirmed allergy to numerous corticosteroids in groups B, D1, and D2, as well a cross-reaction to mometasone furoate. Cross-reactions to Desoxi (Taro Pharmaceuticals Inc., Brampton [ON], Canada) cream and Topicort (Dermik Laboratories, Mississauga [ON], Canada) cream (group C) were also identified, and additional patch testing with 1% and 0.1% desoximetasone in petrolatum (Dermik Laboratories) confirmed that this was a specific reaction to the steroid component. The patient's only reaction to allergens on the European Standard tray was to balsam of Peru. He did not react to any components of the preservative tray.

Discussion

Contact hypersensitivity to corticosteroids occurs in up to 6% of patch-tested patients^{7,8} and has been identified as a

problem of considerable clinical relevance. Patients with allergy to a given corticosteroid may have positive patch-test reactions to a limited number of additional steroids; these are usually corticosteroids with similar molecular structures (ie, Coopman group; see Fig 1).² Cross-reactions between corticosteroid groups are seen with some group A, B, and D corticosteroids. Group C corticosteroids are less frequently involved in corticosteroid cross-reactions.⁹

The intrinsic ability of a given corticosteroid to bind arginine has been identified as an important determinant in its ultimate allergenicity.⁷ Halogenated steroids, especially those with B-ring halogenation and C16-methylation, such as desoximetasone (see Fig 1), have a low binding affinity for arginine and are less allergenic than are corticosteroids in other groups.⁸ Desoximetasone topical allergy was reported in only 6 of 3,016 (0.20%) routine patch-tested patients in Switzerland¹⁰ and in 3 of 106 (2.83%) and 2 of 131 (1.5%) patients with a previously known allergy to one or more corticosteroids.^{11,12} In addition, none of the approximately 500 patients who have undergone patch testing at our institution in the last year have had positive test reactions to 1% desoximetasone in petrolatum.

Table 1. Patch Test Results

<i>Corticosteroid Name</i>	<i>Commercial Preparation</i>	<i>Steroid Group</i>	<i>96-hr Result</i>
Tixocortol pivalate (1% in pet.)		A	—
Hydrocortisone	Prevex HC cream (0.01%)	A	—
Hydrocortisone	Emocort (2.5%) lotion	A	—
Budesonide (0.1% in pet.)		B	1+
Flucinonide	Lidex cream (0.05 %)	B	1+
Amcinonide (0.1% in pet.)		B	1+
Amcinonide	Cyclocort cream (0.1 %)	B	1+
Halcinonide	Halog cream (0.1%)	B	1+
Triamcinolone acetonide (0.1% in pet.)		B	+/-
Desoximetasone	Topicort cream (0.05%)	C	1+
Desoximetasone	Desoxi cream 0.05%	C	2+
Desoximetasone (1% in pet.)		C	1+
Desoximetasone (0.1% in pet.)		C	1+
Mometasone furoate	Elocom cream (0.1 %)	D1	1+
Betamethasone-17-valerate (0.12 % in pet.)		D1	1+
Betamethasone-17-valerate	Prevex B cream (0.1 %)	D1	1+
Clobetasol-17-propionate (0.25 % in pet.)		D1	1+
Clobetasol-17-propionate	Dermovate cream (0.05%)	D1	2+
Halbetasol propionate	Ultravate ointment (0.05%)	D1	2+
Difluocortolone valerate	Nerisone cream (0.1 %)	D1	1+
Hydrocortisone-17-butyrate (0.1 % in pet.)		D2	+/-
Prednicarbate	Dermatop cream (0.1 %)	D2	1+
Hydrocortisone-17-valerate	Westcort cream (0.2 %)	D2	1+
Hydrocortisone-17-valerate	Hydroval cream (0.2 %)	D2	1+

pet = petrolatum.

The structural basis for cross-reaction patterns remains to be fully understood. The corticosteroid D ring was regarded by Coopman and colleagues to be most relevant in predicting cross-reaction patterns.¹ In contrast, Wilkinson and colleagues suggested that C6 and C9 halogenation of the B ring was likely a more important determinant.³ In support of this observation, we noted that in the literature, patients who have cross-reactions to the C6-halogenated desoximetasone frequently have negative patch-test reactions to the nonhalogenated group A corticosteroids (Table 2). Of 8 patients reported in the literature as having cross-reactions to desoximetasone (see Table 2), only 1 had a positive patch-test reaction to a group A corticosteroid.^{4,12–16} Two additional reports describe desoximetasone allergy in two patients who were sensitized by previous use of desoximetasone.^{17,18} One patient had a positive reaction to hydrocortisone as well as to other group A steroids¹⁷ whereas the second patient did not react to patch testing with hydrocortisone.¹⁸ Our patient's negative patch-test reaction to tixocortol pivalate is likely more relevant than the negative patch-test reaction to hydrocortisone, given that detection of hydrocortisone

sensitivity is more reliably made via intradermal injection.¹⁹ It is unlikely that the patient's negative reaction to hydrocortisone is a false negative, given that tixocortol itself is a sensitive and specific marker for hydrocortisone sensitivity. Patients described in the literature as having cross-reactions to various other group C corticosteroids do not appear to have such consistent findings with respect to the negative group A test results. It remains to be determined whether this pattern of negative patch-test reactions to group A corticosteroids is specific for desoximetasone. It is likely that numerous sites of immune recognition on the steroid molecule, rather than a single site, are involved in the establishment of cross-reaction patterns.²⁰

Our patient had a cross-reaction to mometasone furoate, a group D corticosteroid. Its C16 methylation and B-ring halogenation subclassify it as a group D1 corticosteroid and contribute to its rare involvement in positive patch-test results. Many patients tolerate mometasone furoate despite other group D1 allergies. Dooms-Goossens and colleagues reported that only 1 of 48 patients with previously known corticosteroid allergy had a positive patch-test reaction to mometasone furoate.²¹ Other rare

Table 2. Cross-Reactions[†] to Desoximetasone Reported in the Literature

Reference	Group C Tested		Previous Treatments	Group A		Group B		Group D1		Group D2	
	+	–		+	–	+	–	+	–	+	–
Current patient	DES		BTB FLU HCV		HCT TXP	AMC BUD FLU HAL		BTB CLP MOM		HCB PRD	
11	DES DEX FCT	BTM FLU	FCT		HCT PDN PRED		AMC BUD DSN FLA FLU HAL TRI		BTB CLP CLB		HCB PRD
14	DES		BTB BCD CLB		HCT TXP PND	BUD FLA FLU HAL TRI HAL		ACD BCD BCV BTB CLB CLD DFV FLP MOM		HCB	
9	DES		unknown		HCT TXP	BUD	DSN FLU HAL TRI		BCD CLB CLP DFV		HCB
9	DES		unknown		HCT TXP		BUD DSN FLU HAL TRI	CLP	BCD CLB DFV		HCB
15	BTB DES DFD DPD		Topical corticosteroids PRED		HCT TXP	AMC BUD DSN FLA FLU HAL TRI		ACD BTB CLP MOM		HCB HCV	
13	DES	HMT	BDI BTB PRA PDN TRI	HCT TXP			AMC BUD FLA HAL TRI	BTB DFV FLP FMP	CLP		HCB
12	DES DFD		multiple agents FLA		HCT	AMC DFD FLA FLU TRI		BTB	BTB		HCV
12	DES		AMC		HCT	AMC TRI		BTB BTB			

[†]Defined as positive patch-test reactions in patients without previous exposure to Desoximetasone.

ACD = alclometasone dipropionate; AMC = amcinonide; BCD = beclomethasone dipropionate; BCV = beclomethasone valerate; BDI = inhaled budesonide, BTB = betamethasone benzoate; BTB = betamethasone dipropionate; BTM = betamethasone; BTB = betamethasone valerate; BUD = budesonide; CLB = clobetasone-17-butyrate; CLD = clobetasol dipropionate; CLP = clobetasol-17-propionate; DES = desoximetasone; DEX = dexamethasone; DFD = diflorasone diacetate; DFV = difluocortolone valerate; DPD = dexamethasone phosphate disodium; DSN = desonide; FCT = fluocortolone; FLA = fluocinolone acetate; FLD = fluocinolone diacetate; FLP = fluticasone propionate; FLU = fluocinonide; HAL = halcinonide; HCB = hydrocortisone butyrate; HCT = hydrocortisone; HCV = hydrocortisone valerate; HMT = halometasone; MOM = mometasone furoate; PDN = prednisolone; PRA = prednisone 21 acetate; PRD = prednicarbate; PRED = oral prednisone; TRI = triamcinolone acetonide; TXP = tixocortol pivalate.

cross-reactions to mometasone furoate have been described.^{22,23} Our patient is one of the few patients reported in the literature who have had positive patch-test reactions to both desoximetasone and mometasone furoate.^{15,16}

The majority of patients who have cross-reactions to desoximetasone and other group C corticosteroids also have positive test reactions to many group B and group D corticosteroids (see Table 2). These patients frequently have a long history of corticosteroid use, along with allergy to many nonsteroidal products. The factors that contribute to polysensitization are poorly understood but may include differences in corticosteroid metabolism or previous sensitization by other steroidal or nonsteroidal products. Our patient reported a long history of sensitivity to adhesive bandages, Cerumenex (PurduePharma, Pickering [ON], Canada) ear drops, and antiperspirants. His patch-testing was positive for balsam of Peru, which is present in fragrances and flavorings. In addition, the patient's long-standing controlled asthma could potentially have provided a mechanism for sensitization from previous use of corticosteroid inhalers.²⁴ Atopy alone may not be a predisposing factor but may contribute indirectly because atopic patients are frequently exposed to many different products throughout a lifetime.

Further study is needed to better understand the sensitizing potential of steroidal and nonsteroidal preparations and to better define the molecular basis for cross-reaction patterns. Our recommendations to the patient included the avoidance of topical corticosteroids unless a situation urgently required their use. Dermatitic eruptions in the future could be managed with the short-term use of a topical calcineurin inhibitor.

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References

- Coopman S, Degreef H, Dooms-Goossens A. Identification of cross-reaction patterns in allergic contact dermatitis from topical corticosteroids. *Br J Dermatol* 1989;121:27-43.
- Lepoittevin JP, Drieghe J, Dooms-Goossens A. Studies in patients with corticosteroid contact allergy: understanding cross-reactivity among different steroids. *Arch Dermatol* 1995;131:31-7.
- Wilkinson SM, Hollis S, Beck HM. Reactions to other corticosteroids in patients with allergic contact dermatitis from hydrocortisone. *Br J Dermatol* 1995;132:766-71.
- Guin JD. Contact hypersensitivity to topical corticosteroids. *J Am Acad Dermatol* 1984;10:773-82.
- Forstrom L, Lassus A, Salde L, Niemi K. Allergic contact eczema from topical corticosteroids. *Contact Dermatitis* 1982;8:128-33.
- Matura M, Goossens A. Contact allergy to corticosteroids. *Allergy* 2000;55:698-704.
- Wilkinson SM, Jones MF. Corticosteroid usage and binding to arginine: determinants of corticosteroid hypersensitivity. *Br J Dermatol* 1996;135:225-30.
- Lauerma A. Screening for corticosteroid contact sensitivity. *Contact Dermatitis* 1991;24:123-30.
- Rietschel RL, Fowler JF. The role of patch testing. In: Rietschel RL, Fowler JF, editors. *Fisher's contact dermatitis*. 4th ed. Baltimore: Williams & Wilkins; 1995. p. 29.
- Bircher A, Thurlimann W, Hunziker T, et al. Contact hypersensitivity to corticosteroids in routine patch test patients. *Dermatology* 1995;191:109-14.
- Boffa MJ, Wilkinson SM, Beck MH. Screening for corticosteroid contact hypersensitivity. *Contact Dermatitis* 1995;33:149-51.
- Burden AD, Beck MH. Contact hypersensitivity to topical corticosteroids. *Br J Dermatol* 1992;127:497-500.
- Dunkel FG, Elsner P, Burg G. Contact allergies to topical corticosteroids: 10 cases of contact dermatitis. *Contact Dermatitis* 1991;25:97-103.
- Bircher AJ, Levy F, Langauer S, Lepoittevin JP. Contact allergy to topical corticosteroids and systemic contact dermatitis from prednisolone with tolerance of triamcinolone. *Arch Derm Venereol* 1995;75:490-3.
- Venning VA. Fluticasone propionate sensitivity in a patient with contact allergy to multiple corticosteroids. *Contact Dermatitis* 1995;33:48-71.
- Chew AL, Maibach HI. Multiple corticosteroid orally elicited allergic contact dermatitis in a patient with multiple topical corticosteroid allergic contact dermatitis. *Cutis* 2000;65:307-11.
- Dooms-Goossens AE, Degreef HJ, Marien KJ, Coopman SA. Contact allergy to corticosteroids: a frequently missed diagnosis? *J Am Acad Dermatol* 1989;21:538-43.
- Brambilla L, Boneschi V, Chiappino G, et al. Allergic reactions to topical desoxymethasone and oral triamcinolone. *Contact Dermatitis* 1989;21:272-3.
- Wilkinson SM, Cartwright PH, English USC. Hydrocortisone: an important cutaneous allergen. *Lancet* 1991;337:761-2.
- Wilkinson SM. Corticosteroid cross-reactions: an alternative view. *Contact Dermatitis* 2000;42:59-63.
- Dooms-Goossens A, Morren M. Results of routine patch testing with corticosteroid series in 2073 patients. *Contact Dermatitis* 1992;26:82-9.
- Belsito DV. Allergic contact dermatitis to topical glucocorticoids. *Cutis* 1993;52:291-4.
- Raasanen L, Tuomi ML. Cross-sensitization to mometasone furoate in patients with corticosteroid contact allergy. *Contact Dermatitis* 1992;27:323-5.
- Kilpio K, Hannuksela M. Corticosteroid allergy in asthma. *Allergy* 2003;58:1131-5.