Steroid Use in Prednisone Allergy

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If a patient has an allergy to prednisone and methylprednisolone, what (if any) other corticosteroid can the patient use to avoid an allergic reaction?

Corticosteroids very rarely cause allergic reactions in patients that receive them. Since corticosteroids are typically used to treat severe allergic reactions and anaphylaxis, it seems unlikely that these drugs could actually induce an allergic reaction of their own. However, between 0.5-5% of people have reported any sort of reaction to a corticosteroid that they have received.[1] Corticosteroids can cause anything from minor skin irritations to full blown anaphylactic shock. Worsening of allergic symptoms during corticosteroid treatment may not always mean that the patient has failed treatment, although it may appear to be so.[2,3]

There are essentially four classes of corticosteroids: Class A, hydrocortisone-type, Class B, triamcinolone acetonide type, Class C, betamethasone type, and Class D, hydrocortisone-17-butyrate and clobetasone-17-butyrate type. Major* corticosteroids in Class A include cortisone, hydrocortisone, methylprednisolone, prednisolone, and prednisone. Major* corticosteroids in Class B include budesonide, fluocinolone, and triamcinolone. Major* corticosteroids in Class C include beclomethasone and dexamethasone. Finally, major* corticosteroids in Class D include betamethasone, fluticasone, and mometasone.[4,5] Class D was later subdivided into Class D1 and D2 depending on the presence or absence of a C_{16} methyl substitution and/or halogenation on C_9 of the steroid B-ring.[5,6]

It is often hard to determine what exactly a patient is allergic to if they experience a reaction to a corticosteroid. Hypersensitivity may occur to the corticosteroid itself or to the stabilizers, preservatives or adjuvants in their preparations. Succinate esters of hydrocortisone are the most frequent culprits of immediate hypersensitivity reactions. There have also been reports of anaphylaxis secondary to the carboxymethylcellulose constituent in steroid suspensions. In fact, three different tests exist to confirm corticosteroid allergies: skin patch, intradermal, and provocation tests. The provocation

**For full list, please see attached sheet.*

test appears to be the most reliable test to identify reactions to corticosteroids as well as to identify safe corticosteroids for future therapy.[7]

Cross-reactivity between corticosteroids is most likely to occur within (NOT between) the 4 structural corticosteroid groups.[4,8] In fact, there have been multiple reports of cross-reactivity among hydrocortisone, methylprednisolone, and prednisone.[7] Cross-reactions are relatively unusual between corticosteroids of different groups. Few adverse reactions have been reported to betamethasone esters or mometasone, so it is advised to recommend these molecules (or ones structurally similar) to patients who demonstrate a sensitivity to other corticosteroids.[4] Budesonide cross-reacts with not only the other corticosteroids in its own class, but also with those in Class D2.[4,5,6] Corticosteroids in Class A are also likely to cross-react with corticosteroids in Class D2.[5,6] Class D1 exhibits low cross-reactivity between the other classes.[6]

Lately, many case studies have surfaced of patients experiencing IgE-mediated allergic-type reactions to succinylated corticosteroids. "Succinylated corticosteroids" refers to corticosteroids with a succinate ester portion such as methylprednisolone sodium succinate and prednisolone sodium succinate. Corticosteroids are "esterified" with succinic acid, phosphoric acid, and other forms to make them more water-soluble. When a corticosteroid is more water soluble, it can be more easily dissolved for intravenous administration. Corticosteroids are most often esterified at the C_{21} position. One patient, who was found to be allergic to methylprednisolone sodium hemisuccinate and prednisolone hemisuccinate, experienced no reaction whatsoever from succinate-free corticosteroids (e.g. dexamethasone sodium phosphate, methylprednisolone without the succinate moiety, and betamethasone).[2] There are many other case studies similar to this which suggests that these patients

are not experiencing an allergic reaction to the corticosteroid moiety itself, but rather to particular formulations of the corticosteroid (i.e. its specific salt form).[1,9,10,11]

In conclusion, prednisone and methylprednisolone are classified as “Class A” corticosteroids. If a patient has an allergic reaction to these two molecules, the patient in question should be advised to avoid all Class A corticosteroids (refer to the chart below). The patient should also be advised to avoid all Class D2 corticosteroids as Class A corticosteroids are likely to cross-react with class D2 corticosteroids. Betamethasone or dexamethasone would be good choices for the patient since these are Class C corticosteroids and have not been shown, to my knowledge, to cross-react with any corticosteroids in Class A.

Classification of Corticosteroids[4,5,6,8]

Class A "Hydrocortisone-type"	**Class B** "Triamcinolone acetonide-type"	**Class C** "Betamethasone-type"	**Class D** "Hydrocortisone- and clobetasone-17-butirate-type"
No substitution on the corticosteroid D-ring or the C_{20}, C_{21}-chain. Includes C_{17} and/or C_{21} short-chain acetate esters.	-*Cis*-ketal or -diol substitution on C_{16}, C_{17} portion. Acetonide group.	C_{16}-methyl substitution and nonesterfied at C_{17}, C_{21}.	Long-chain ester at C_{17} and/or C_{21} and with or without a C_{16}-methyl substitution. Ester group.
Cloprednol	Amcinonide	Beclomethasone hydrochloride	Alclomethasone dipropionate (D1)
Cortisone acetate	Budesonide	Betamethasone	Beclomethosone dipropionate (D1)
Fludrocortisone acetate	Desonide	Betamethasone sodium phosphate	Betamethasone valerate (D1)
Fluormetholone	Flucloronide	Dexamethasone	Clobetasone-17-butyrate (D1)
Fluormetholone acetate	Flunisolide	Dexamethasone acetate	Clobetasol propionate (D1)
Fluorprednisolone acetate	Fluocinolone acetonide	Dexamethasone disodium phosphate	Diflucortolone valerate
Hydrocortisone	Fluocinonide	Dexamethasone isonicotinate	Flumethasone pivalate
Hydrocortisone acetate	Formocortal	Dexamethasone metasulfobenzoate	Fluticasone propionate (D2)
Hydrocortisone succinate	Halcinonide	Dexamethasone sodium phosphate	Hydrocortisone aceponate (D2)
Isoflupredone acetate	Procinonide	Desoximethasone	Hydrocortisone-17-butyrate (D2)
Medrysone	Triamcinolone and esters	Diflorason diacetate	Hydrocortisone-17-propionate (D2)
Meprednisone	Triamcinolone acetonide	Flucortin butyl	Hydrocortisone-17-valerate (D2)
Methylprednisolone		Fluocortolone and esters	Methylprednisolone aceponate (D2)
Methylprednisolone acetate		Halomethasone	Mometasone furoate (D2)
Methylprednisolone hemisuccinate			Prednicarbate (D2)
Methylprednisolone sodium phosphate			
Prednisolone (and salts)			
Prednisone			
Tixocortol pivalate			

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