

Ann Allergy . 1985 Oct; 55(4): 588-600

a communication from Canada

ANAPHYLACTIC RESPONSE TO HYDROCORTISONE IN CHILDHOOD: A CASE REPORT

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Anaphylactic reactions to hydrocortisone have been well described in adults, but have not been reported in children. We wish to report such a reaction in a 6-year-old girl who had a positive intradermal reaction to methylprednisolone. Control subjects were non-reactive. Previous literature is briefly reviewed and discussed.

High-dose steroids are extensively used in the management of acute bronchospasm due to asthma or other allergic phenomena. Corticosteroids, particularly hydrocortisone (HC) and methylprednisolone (MP), have been implicated in rare anaphylactic reactions in adolescents and adults.¹⁻⁹ A clinical association between these adverse reactions and aspirin (ASA) sensitivity has been suggested,⁸ and bronchospastic response to hydrocortisone has been demonstrated in adult ASA-sensitive asthmatics.¹⁰ We report a case of anaphylaxis due to intravenous hydrocortisone succinate (HC-S) in a 6-year-old girl, and review the literature on steroid anaphylaxis as it relates to the optimal selection of corticosteroids.

Case Report

The patient was a 6-year-old white female with a long standing history of severe asthma, eczema, and chronic allergic rhinitis. She suffered from multiple food and inhalant allergies and has had positive intradermal skin testing for many foods, pollens, and animal derivatives. She had received oral and intravenous steroids on a large number of occasions, but was not receiving steroids immediately prior to her presentation. While on a camping trip she developed an exacerbation of her asthma and was seen at another institution where an intravenous infusion was begun. Theophylline was uneventfully administered by intravenous bolus. Subsequently, the patient was given 150 mg of intravenous HC-S (Solu-Cortef, Upjohn, contents = hydrocortisone succinate, water, and sodium phosphate buffer).¹¹ Within several minutes she began to complain of itching in the throat followed by severe shortness of breath and diffuse urticaria. She responded well to intravenous epinephrine and diphenhydramine, and was transferred

for urticarial reactions to numerous food items. Aspirin had been avoided without documented sensitivity. Except for her allergies and eczema she was in good general health.

Family history indicated only allergy to grasses in the father, who was adopted. There were no siblings.

Physical examination revealed a weight and height less than the third percentile, an increased A-P chest diameter, auscultatory findings consistent with resolving asthma and eczema.

The patient's acute exacerbation resolved uneventfully following treatment with per oral prednisone, theophylline, and beta-agonists. Three days following her presentation she and her parents were subjected to intradermal skin testing using 0.02 mL doses of various commercially available intravenous preparations. The parents do not suffer from eczema. Results are shown in the Table. The subject was not available for further *in vitro* investigations.

Discussion

While anaphylaxis following the systemic administration of steroids is quite rare, there are at least 14

Table. Intradermal Skin Test Results Using 0.02 mL of Undiluted Injectable Preparations*

	Patient Ery- thema/ Wheal (mm)	Mother	Father	Excipients
HC-S (125 mg/ mL)	10/3	—	—	Sodium phosphate (11)
MP-S (125 mg/ mL)	20/5	—	—	Sodium phosphate (11)
Dexametha- sone (4 mg/ mL)	5/0	—	—	Sodium metabisulfite & parabens (12)

* HC-S = hydrocortisone succinate and MP-S = methylprednisolone

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documented cases in the literature.¹⁻⁹ All of these patients were adults and most were chronically atopic individuals with prior steroid exposure. In addition, ASA sensitivity was noted in two cases⁸ and has been postulated as a risk factor for steroid anaphylaxis.

Our patient, who was highly atopic, appears to have suffered an acute anaphylactic reaction to a preparation containing only HC-S and inorganic buffers. Skin testing resulted in an equivocal response to HC-S and a definite positive response to MP-S. The poor response to HC-S may be due to the very recent anaphylaxis or to poor skin test reactivity of the HC-S skin test material. Cross reactivity between HC-S and MP-S was reported by Mendelson et al⁵ in a patient who reacted clinically to both drugs and also by Freedman et al¹³ in a patient who had reacted to MP-S. Mendelson et al were able to demonstrate positive skin testing to HC and MP, but could not achieve reliable skin testing with the succinate esters. They speculated that a small amount of de-esterified impurity in commercial preparations may be the offending agent in some cases. The possibility of a non-immune mechanism (similar to the histamine releasing effects of morphine) has also been suggested based upon the inability to demonstrate passive transfer to immunity,^{4,5} complement consumption,⁵ serum antibody,⁴ or histamine release.⁴

Interestingly, our patient did not react to per oral prednisone or intradermal dexamethasone. This is consistent with the literature experience that prednisone and dexamethasone have never been reported to cause anaphylactic or intradermal wheal reactions.

A further bit of intriguing information is the isolated observation of DeJani et al,¹⁰ who investigated the pulmonary response of 12 ASA-sensitive adult asthmatics to HC-S, dexamethasone, and placebo. Three of these patients had significant (18% to 48%) falls in FEV₁ after intravenous HC-S. None of the patients responded to dexamethasone or placebo, and none had other evidence of immune response clinically or by intradermal testing. The use of the succinate esters for intradermal testing and the lack of a normal and/or ASA non-sensitive asthmatic control group make it difficult to draw conclusions regarding the roles of immune response and ASA sensitivity. The paper does suggest the possibility, however, that some asthmatics may react adversely to intravenous HC-S.

In summary, the available literature would suggest that steroids—especially HC, MP, and their succinate

esters—may be associated with anaphylactic reactions. Additionally, a number of asthmatics may have a bronchospastic response to intravenous hydrocortisone but not to dexamethasone. The role of aspirin sensitivity in determining the risk of bronchospastic or anaphylactic responsiveness remains unclear. Intravenous prednisone and dexamethasone appear to have less of a tendency to induce anaphylactic responses; but this may be an artifact due to less frequent use.

Clearly, one must consider adverse reactions to steroids in the differential diagnosis of bronchospasm which fails to respond to therapy. Alternative therapy with dexamethasone or prednisone may be indicated, especially in ASA-sensitive patients. Generalization of these recommendations to the asthmatic population at large will require better definition of the side effects of individual corticosteroids.

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