# An anaphylactic reaction to intra-articular triamcinolone: a case report and review of the literature

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**Objective:** The primary objective was to report a case of triamcinolone-induced anaphylaxis and review the proposed mechanisms of corticosteroid-associated hypersensitivity reactions.

**Data Sources:** Articles in French and English were identified from references in relevant articles and from articles retrieved from the PubMed web site. Indexing terms consisted of corticosteroids in conjunction with the terms anaphylaxis, hypersensitivity reactions, asthma, urticaria, and angioedema.

**Study Selection:** We reviewed all articles that described a case or cases of allergic-type reaction in association with corticosteroid use and for which we could obtain the full text of the article (>95%).

**Results:** We report an anaphylactic reaction occurring after an intraarticular injection of triamcinolone in a 75-year-old man who had positive prick skin tests to triamcinolone and negative tests to lidocaine, methylprednisolone, and hydrocortisone.

**Conclusions:** To date, there have been approximately 100 published reports of immediate hypersensitivity reactions occurring after oral and parenteral administration of corticosteroids. Both immunologic and nonimmunologic mechanisms are proposed, but there is no definitive evidence in favor of either hypothesis. Our patient demonstrated positive prick skin tests to triamcinolone in a dose-response manner, suggesting the likelihood that an immunoglobulin E-mediated hypersensitivity mechanism may play a role.

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## INTRODUCTION

The common side effects of corticosteroids are well known. Among the uncommon side effects of the drug is the development of immediate hypersensitivity reactions such as hives, angioedema, and/or anaphylaxis, which have been reported after oral and parenteral administration.[1] It is ironic that the medication most used to treat severe allergic diseases has itself been associated with severe immediate hypersensitivity reactions.

Hypersensitivity reactions to intraarticular and periarticular cortisone were noted early. In fact, the results of these initial studies are the only systematic assessments of the rate of these adverse reactions to steroids. In 1953, Brown et al[2] reported urticaria in 4 of 547 treated patients [0.7%]. Half a decade later, Kendall[3] reported allergic-type reactions in 20 of 2,256 patients [0.9%] (urticaria at injection site in 11, generalized urticaria in 8, and bronchospasm and angioedema in 1 asthmatic patient). These authors were reluctant to blame the steroid and attributed the allergic manifestations to additives or vehicles used with the steroid such as procaine or hyaluronidase.[2,3] For example, three of the four patients reported by Brown et al with urticaria had positive wheal and flare reactions to intradermal tests with procaine.

O'Garra[4] was one of the first to blame the steroid itself, although the scientific basis for the conclusion is somewhat tenuous. Of three patients whose dyspnea began at least 4 hours after injection of a plantar fasciitis with hydrocortisone acetate, one patient tested positive to skin testing with purified hydrocortisone containing no additives and did not react to the vehicle. Although evidence supports the concept that the steroid itself is the cause of the allergic-type reaction,[1] there is ongoing debate about the mechanism of the reaction.

We describe a patient who developed an anaphylactic reaction to intraarticular triamcinolone and who demonstrated positive skin prick tests to triamcinolone and negative skin prick tests to methylprednisolone and hydrocortisone. We review the literature of allergic reactions to corticosteroids and discuss the possible mechanisms underlying such reactions.

## CASE REPORT

A 75-year-old man received an injection of a mixture of 80 mg triamcinolone (Kenalog, Westwood-Squibb, Montreal, Quebec, Canada) and 1% carbocaine into the right shoulder for bursitis. Within 10 minutes, he began to feel "very bad" and developed urinary incontinence, syncope, and generalized hives. He was noted to be short of breath, with rigors and cyanosis of the hands. The blood pressure was 65 mm Hg systolic, pulse was 110 beats/minute, and the respiration rate was 20 breaths/minute. The diagnosis of anaphylaxis was made and the patient was treated with intravenous fluids, diphenhydramine hydrochloride (Benadryl, Pfizer, Morris Plains, NJ), and adrenaline.

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The patient's medical history included a myocardial infarction 2 years earlier. He also had a hiatus hernia and hyperlipidemia. Concurrent medications were pravastatin sodium (Pravachol, Squibb), 20 mg daily, and ranitidine, 150 mg, twice daily. He had an uneventful intraarticular injection into the same shoulder 20 years ago with an unknown corticosteroid. In the past, he had allergic reactions to penicillin and bee stings. Six weeks after the reaction, the patient had negative skin prick tests to xylocaine, carbocaine, novocaine, marcaine, prilocaine, and ultracaine. A subcutaneous provocative challenge test to 1 mL of 1% carbocaine was negative. Skin prick tests to dilute commercial Kenalog (triamcinolone 1 mg/mL) and the histamine control were positive and the saline control test was negative. A week later the patient was retested by skin prick test to several commercial steroid preparations (Table 1). The patient reacted only to triamcinolone in a dose-dependent manner (Fig 1). The histamine skin test control resulted in a wheal of 2 mm, and the saline control was negative. Skin prick tests with triamcinolone 1 mg/mL were negative in 13 normal volunteers.

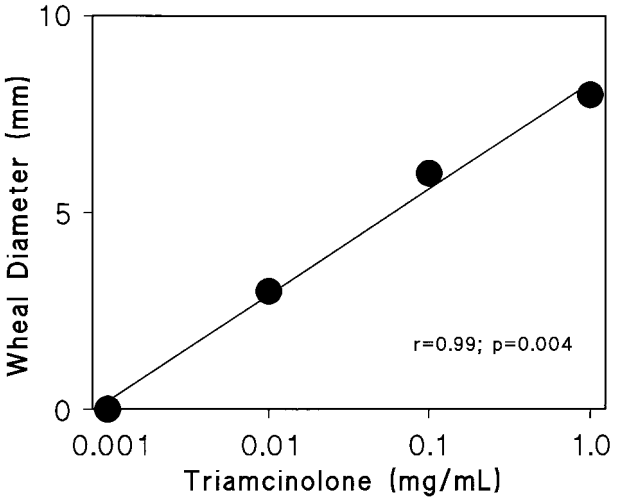

Figure 1. Results of skin prick testing with triamcinolone.

## DISCUSSION

Shortly after the first demonstrations of the antiinflammatory effects of cortisone in rheumatoid arthritis, Carryer et al[5] reported the antiallergic effects of cortisone in patients with hay fever and asthma. Thus, the first observations of hypersensitivity reactions to corticosteroids were met with skepticism and attributed to the vehicle or other components concomitantly injected.[2,3] However, the results of several investigated cases support the concept that the steroid itself is the culprit. Several warrant elaboration.

Comaish[6] described a patient who twice had episodes of hives after oral prednisone and one episode several hours after an intra-articular injection of prednisolone acetate. Intradermal skin tests were positive at 3 hours or later for prednisolone acetate, prednisone, and hydrocortisone and negative for the other components of the injected material. Comaish purified preparations of steroids obtained from Medical Research Council Steroid Reference Collection until each moved as a single line on paper and thin layer chromatography and again demonstrated positive intradermal skin tests to prednisolone acetate and hemisuccinate, hydrocortisone hemisuccinate, and free hydrocortisone.

Mendelson et al[7] studied a 17-year-old patient with poorly controlled asthma in whom generalized urticaria and angioedema developed, and whose asthma worsened, leading to three hospital admissions for status asthmaticus, after receiving intravenous Solu-Cortef or Solu-Medrol (The Upjohn Company, Kalamazoo, MI). When the asthma was controlled, intradermal skin tests with a 1:100 dilution of Solu-Medrol (final concentration of methylprednisolone sodium succinate 0.4 mg/mL) and Solu-Cortef (dose unspecified) were performed and were negative at 20 minutes and at 3 hours posttest. Intravenous challenges with 40 mg of Solu-Medrol (containing methylprednisolone sodium succinate and preservatives including methylparaben and propylparaben) produced symptoms within 2 minutes; preservative-free methylprednisolone sodium succinate produced symptoms (urticaria, angioedema, and asthma) within 11 minutes; and oral challenge with 40 mg of plain methylprednisolone produced symptoms within 35 minutes. In contrast, intravenous challenges with the preservatives in Solu-Medrol, lower intravenous 4-mg doses of Solu-Medrol and methylprednisolone sodium succinate, and oral challenges with 40 mg prednisone and prednisolone and 6 mg dexamethasone were negative. The authors performed another extensive series of intradermal skin tests. They again noted negative intradermal tests to Solu-Medrol and methylprednisolone sodium succinate (which had provided positive intravenous challenges), methylprednisolone sodium acetate, prednisolone, prednisone, dexamethasone, triamcinolone, Solu-Cortef, hydrocortisone sodium succinate, cortisone acetate, and the preservatives for Solu-Medrol. In contrast positive immediate reactions were obtained with methylprednisolone tablets and powder and hydrocortisone tablets and powder. The authors reconciled the inconsistent results of the various oral, intravenous, and intradermal skin challenges by concluding that the patient reacted to small amounts of unconjugated steroids present in the Solu-Medrol and Solu-Cortef preparations.

Pryse-Phillips et al[8] described a 53-year-old man with multiple sclerosis in whom urticaria, angioedema, and anaphylaxis developed within 2 minutes of starting a 1,000-mg

Table 1. Results of Skin Prick Tests* to Corticosteroids

| | Triamcinolone (10 mg/mL) | Methylprednisolone (40 mg/mL) | Hydrocortisone (50 mg/mL) |
|---|---|---|---|
| Dilution | | | |
| 1/10 | 8 | 0 | 0 |
| 1/100 | 6 | 0 | 0 |
| 1/1000 | 3 | 0 | 0 |
| 1/10,000 | 0 | 0 | 0 |

* Skin prick results are shown as wheal size in millimeters.

intravenous pulse of Solu-Medrol (methylprednisolone sodium succinate). The estimated dose received was 11 mg. In support of an immunologic reaction, the authors stated that the patient had a positive radioallergosorbent test (RAST) for specific immunoglobulin (Ig)E antibodies to methylprednisolone, a positive skin prick test to methylprednisolone, a negative prick test to hydrocortisone, and a positive passive cutaneous anaphylaxis test (transfer by serum of positive reactivity to a control).

Mace et al[1] described a 31-year-old woman who had inflammatory polyarthritis and in whom angioedema and anaphylaxis developed within 10 seconds of an intraarticular knee injection of 1 mL of 2% lidocaine and 80 mg methylprednisolone acetate. A similar injection 4 years earlier had been uneventful. Four weeks after the reaction, skin prick testing with commercial preparations of methylprednisolone acetate (40 mg/mL), hydrocortisone sodium succinate (50 mg/mL), betamethasone acetate (6 mg/mL), dexamethasone sodium phosphate (4 mg/mL), triamcinolone acetonide (40 mg/mL), lidocaine, and raw latex were negative. In contrast, an intradermal test to 40 mg/mL of methylprednisolone acetate was strongly positive (10-mm wheal) but intradermal tests to lower concentrations of methylprednisolone acetate (5,10, 15, and 20 mg/mL) were negative. Negative intradermal tests were obtained to constituents in the commercial methylprednisolone acetate preparation, lidocaine, and other commercial steroid preparations (betamethasone, triamcinolone, and dexamethasone). A positive intradermal test was noted for hydrocortisone. A repeat intradermal test at an unspecified later date using 40 mg/mL methylprednisolone acetate resulted in chest tightness, generalized itch, urticaria, and tachycardia.

In addition to the publications above, there have been numerous additional reports of one or several cases of immediate-type hypersensitivity reactions to corticosteroids.[9–50] The topic has been reviewed on several occasions.[51,52] To date, the cumulative number of patients experiencing such reactions is less than 100.

How corticosteroids cause immediate-type hypersensitivity reactions is unknown. Both immunologic and nonimmunologic mechanisms, for example direct triggering of mast cells, have been proposed. Analogous to other immediate-type hypersensitivity reactions, an IgE-mediated mechanism is favored but definitive evidence for such a mechanism in corticosteroid induced reactions is lacking. Pryse-Phillips et al[8] are the only authors to report a positive passive cutaneous anaphylaxis test (presumed transfer of reaction by serum antibodies) and a positive RAST for specific IgE-methylprednisolone antibodies. Unfortunately, they provided no details about the assay or the controls that were used. In contrast, Mendelson et al[7] were unable to transfer steroid sensitivity to three different recipients despite successfully simultaneously transferring their patient's sensitivity to Bermuda grass. Fulcher et al[39] reported a negative RAST to the presumed corticosteroid antigen. RASTs using steroid molecules to detect specific IgE antibodies are technically difficult assays[1] and have seldom been performed during the evaluation of patients with allergic-like reactions to corticosteroids. Part of the difficulty lies in the nature of the allergen. Corticosteroid molecules most likely act as haptens, and the protein-steroid complex that is most likely the allergen is unknown and unavailable as a reagent.

In place of the direct demonstration of antigen-specific IgE antibodies, skin tests resulting in an immediate wheal and flare reaction are a well established surrogate measure of an IgE-mediated mechanism.[53] Patients should be evaluated first by the more specific but less sensitive prick test followed by intradermal testing if prick tests are negative. Intradermal tests have a higher rate of nonspecific (false-positive) reactions, especially when higher concentrations are used, and they are more likely to induce anaphylactic-like reactions. Patients should be tested against the steroid preparation that is the presumed cause of the reaction, and with other steroid preparations used as a control. In this way, a steroid might be identified that could be used therapeutically. When performed, skin tests were positive in 19 of 25 (76%) cases of systemic reactions[52]; negative intradermal tests correlated with the ability to tolerate an alternative steroid preparation.[7,11,20,34,38,39] Because not all patients with corticosteroid-induced reactions have been studied systematically, the sensitivity, specificity, and positive and negative predictive values of skin tests in patients with steroid-induced hypersensitivity reactions remain unknown.

The clinical and laboratory features of our patient support an IgE-mediated mechanism. First, the reaction was typical of an anaphylactic reaction, occurring within 10 minutes of receiving the intraarticular injection and characterized by hypotension, shortness of breath, generalized hives, and cyanosis. Second, the patient demonstrated a clear wheal and flare reaction to skin prick testing with diluted triamcinolone that was reproducible (repeated on two separate occasions). He also demonstrated a dose-response curve (Fig 1), and the specificity was supported by negative (saline, other corticosteroid preparations) and positive (histamine) controls.

Provocative challenges (oral, intramuscular, subcutaneous, and intravenous) have been used in some cases to demonstrate reactivity to corticosteroids. This approach does not address the mechanism of the reaction, but it is useful to confirm that the patient may be reactive.[7,20]

The antigen that causes corticosteroid-induced immediate hypersensitivity is not established. In this study and others, preservatives in commercial corticosteroid preparations such as parabens and metabisulfites have been excluded, as have topical anesthetics coadministered in intraarticular injections.[1,7,12] No single corticosteroid molecule structure has been identified as possibly leading to immediate hypersensitivity reactions. Immediate reactions have been described following all sorts of corticosteroid molecules (hydrocortisone, methylprednisolone, triamcinolone, dexamethasone) and preparations (succinate, acetate and phosphate formulations). The rarity of reports for some corticosteroids likely reflects the hierarchy of steroid use in practice rather than

suggesting a steroid structure unlikely to cause a reaction. The corticosteroid molecule may in fact not be the immunogen. It is likely that the corticosteroid molecule combines with serum or tissue proteins or enzymes to form immunogenic steroid-protein-enzyme conjugates with the corticosteroid acting as the hapten against which the IgE response is directed.

Many reactions have occurred in patients with asthma. The preponderance of asthmatic patients may reflect selection bias imposed by the frequent treatment of patients with poorly controlled asthma with intravenous corticosteroids. However, this observation in combination with the knowledge that corticosteroids are inhibitors of prostaglandin production has led to the hypothesis that the mechanism of corticosteroid-induced hypersensitivity reactions is nonimmunologic and is identical to the mechanism of aspirin-induced asthma (AIA) and anaphylaxis. Indeed, several authors noted that patients with corticosteroid-induced immediate hypersensitivity reactions were also intolerant of aspirin.[15,20,47,50] However, the results of intravenous steroid challenges in patients with AIA have been contradictory. Only 1 of 45 patients with AIA challenged by Feigenbaum et al[54] and 3 of 11 challenged by Dajani et al[20] with 100 mg of intravenous hydrocortisone sodium succinate experienced bronchospasm. In contrast, Szczeklik et al[55] reproduced immediate falls in forced expiratory volume in 1 second in 31 patients with AIA who were challenged with 300 mg intravenous hydrocortisone, although only 3 of the patients had clinical symptoms of bronchospasm. None of the three responded to intravenous methylprednisolone, dexamethasone, or betamethasone.

AIA is a well established nonimmunologic model of hypersensitivity.[56] The mechanism appears to relate to overproduction of bronchoconstricting leukotrienes.[57] Drugs implicated in AIA share the property of cyclo-oxygenase inhibition. Unfortunately, the results of the aforementioned intravenous hydrocortisone challenge studies do not comprehensively address the question of mechanism of steroid-induced asthma. Too few patients have been challenged with multiple forms of corticosteroid preparations to address the question of a steroid class affect. Most challenges were performed before it was known that the mechanism of AIA relates to alterations in prostanoid metabolism and provide no assessments of prostanoid production in vivo by patients undergoing challenge. Beynel et al[45] evaluated three patients with immediate hypersensitivity reactions to corticosteroids and positive prick and intradermal skin tests with an in vitro challenge assay of leukotriene $C_4$ production and describe positive results in all three. Nevertheless, the results of these studies fall far short of a comprehensive evaluation of mechanism and appear to muddy the picture rather than shed light.

The administration of corticosteroids, regardless of type or route of administration, is associated with a finite risk of a hypersensitivity reaction. The mechanism is unclear, but skin test results provide stronger evidence in support of an immunologic IgE-mediated mechanism than the results of intravenous hydrocortisone challenges, which support a pharmacologic affect akin to AIA. It is possible that both immunologic and nonimmunologic mechanisms may be responsible in different patients. Both mechanisms have been noted among specific patients with urticaria and anaphylactoid reactions induced by aspirin or nonsteroidal antiinflammatory drugs (NSAIDs).[56] That is, some patients react to a single NSAID, presumably by means of an IgE-mediated mechanism, and others react to several NSAIDs, presumably by means of a class effect involving cyclooxygenase inhibition and leukotriene overproduction. Negative skin tests appear to predict the safe use of alternate steroid preparations, although the absolute safety of this approach has not been conclusively ascertained. Rheumatologists must be prepared to treat patients who have anaphylactic reactions in clinics and offices where intramuscular and intraarticular injections are performed.

## REFERENCES


1. Mace S, Vadas P, Pruzanski W. Anaphylactic shock induced by intraarticular injection of methylprednisolone acetate. J Rheumatol 1997;24:1191–1194.
2. Brown EM, Frain JB, Udell L, Hollander JL. Locally administered hydrocortisone in the rheumatic diseases. Am J Med 1953;15:656–665.
3. Kendall PH. Untoward effects following local hydrocortisone injection. Ann Phys Med 1958;4:170–175.
4. O'Garra J. Anaphylactic reactions to hydrocortisone injections. BMJ 1962;1:615.
5. Carryer HM, Koelsche GA, Prickman LE, et al. The effects of cortisone on bronchial asthma and hay fever occurring in subjects sensitive to ragweed pollen. J Allergy 1950;21:282.
6. Comaish S. A case of hypersensitivity to corticosteroids. Br J Dermatol 1969;81:919.
7. Mendelson LM, Meltzer EO, Hamburger RN. Anaphylaxis-like reactions to corticosteroid therapy. J Allergy Clin Immunol 1974;54:125–131.
8. Pryse-Phillips WE, Chandra RK, Rose B. Anaphylactoid reaction to methylprednisolone pulsed therapy for multiple sclerosis. Neurology 1984;34:1119–1121.
9. King RA. A severe anaphylactoid reaction to hydrocortisone. Lancet 1960;2:1093–1094.
10. Maddin S. Urticaria following betamethasone. J Am Med Assoc 1969;207:560.
11. Von Maur K, Rocklin R, Stevens M. Corticosteroid allergy in a patient with systemic lupus erythematosus. Johns Hopkins Med J 1974;134:356–364.
12. Tannenbaum H, Ruddy S, Schur PH. Acute anaphylaxis associated with serum complement depletion. J Allergy Clin Immunol 1975;56:226–234.
13. Kounis NG. Untoward reactions to corticosteroids: intolerance to hydrocortisone. Ann Allergy 1976;36:203–206.
14. Romankiewicz JA, Franklin JE Jr. Allergic reactions to corticosteroid therapy. J Am Med Assoc 1976;236:1939.
15. Partridge M, Gibson G. Adverse bronchial reactions to intravenous hydrocortisone in two aspirin sensitive patients. BMJ 1978;1:1521–1522.
16. Hayhurst M, Braude A, Benatar S. Anaphylactic-like reactions to hydrocortisone. S Afr Med J 1978;53:259–260.
17. Chapman S, Loughnan B, Somerfield S. Immediate hypersensitivity skin testing in a case of hydrocortisone anaphylaxis: case report. N Z Med J 1979;90:380.
18. Ward K, Prichard J. Severe bronchial reaction and cardiopul-

monary arrest following intravenous injection of hydrocortisone in a non-atopic, non-aspirin-sensitive asthmatic. Irish J Med Sci 1980;149:124–126.
19. Ashford R, Bailey A. Angioneurotic oedema and urticaria following hydrocortisone–a further case. Postgrad Med J 1980;56:437.
20. Dajani BM, Sliman N, Shubair K, Hamzeh YS. Bronchospasm caused by intravenous hydrocortisone sodium succinate (Solucortef) in aspirin-sensitive asthmatics. J Allergy Clin Immunol 1981;68:201–204.
21. Freedman M, Schocket AL, Chapel N, Gerber JG. Anaphylaxis after intravenous methylprednisolone administration. J Am Med Assoc 1981;245:607–608.
22. Rao KV, Anderson RC, O'Brien TJ. Successful renal transplantation in a patient with anaphylactic reaction to Solu-medrol (methylprednisolone sodium succinate). Am J Med 1982;72:161–163.
23. Rodger R. Anaphylaxis following treatment with a corticosteroid: report of one case. Clin Allergy 1983;13:499–500.
24. Thompson JF, Chalmers DH, Wood RF, et al. Sudden death following high dose intravenous methylprednisolone. Transplantation 1983;36:594–596.
25. Becq H, Dequeker J. Hypersensitivity reaction to pulse dose of methylprednisolone (solumedrol): a case report. Acta Clinica Belgica 1983;38:262–264.
26. Shu Chan C, Brown IG, Oliver WA, Zimmerman PV. Hydrocortisone-induced anaphylaxis. Med J Aust 1984;141:444–446.
27. Seale JP. Anaphylactoid reaction to hydrocortisone. Med J Aust 1984;141:446.
28. Clee M, Ferguson J, Browning M, et al. Glucocorticoid hypersensitivity in an asthmatic patient: presentation and treatment. Thorax 1985;40:477–478.
29. Peller J, Bardana E. Anaphylactoid reaction to corticosteroid: case report and review of the literature. Ann Allergy 1985;54:302–305.
30. Goldstein D, Zimmerman B, Speilberg S. Anaphylactic response to hydrocortisone in childhood: a case report. Ann Allergy 1985;55:599–600.
31. Mansfield L, Ting S, Haverly R. Anaphylaxis caused by the sodium succinate ester of hydrocortisone and methylprednisolone. J Asthma 1986;23:81–83.
32. Mcnamara R. Anaphylaxis after intravenous corticosteroid administration. J Emerg Med 1987;4:213–215.
33. Egashira K, Origuchi H, Sagara T, Kikuchi Y. Coronary artery spasm during hydrocortisone induced allergic reactions. Am Heart J 1987;113:1516–1517.
34. Dozema D. Anaphylaxis following administration of intravenous methylprednisolone sodium succinate. Am J Emerg Med 1987;5:42–44.
35. Al-Mahdy H, Hall M. Anaphylaxis and hydrocortisone. Ann Intern Med 1988;108:487–488.
36. John GT, Thomas PP, Kirubakaran M, et al. Methylprednisolone sodium succinate-induced anaphylaxis in a nonatopic renal transplant patient. Transplantation 1989;48:543.
37. Larrson LG. Anaphylactic shock after i. a. administration of triamcinolone acetonide in a 35-year-old female. Scand J Rheumatol 1989;18:441–442.
38. Sieck JO, al-Ohaly Y, Saour J, et al. An allergic reaction to intravenous methylprednisolone administration. Br J Clin Pract 1990;44:723–725.
39. Fulcher D, Katelaris C. Anaphylactoid reaction to intravenous hydrocortisone sodium succinate: a case report and literature review. Med J Aust 1991;154:210–214.
40. Murrieta-Aguttes M, Michelen V, Leynadier F, et al. Systemic allergic reactions to corticosteroids. J Asthma 1991;28:329–339.
41. Lopez-Serrano MC, Moreno-Ancillo A, Contreras J, et al. Two cases of specific adverse reactions to systemic corticosteroids. J Investig Allergol Clin Immunol 1996;6:324–327.
42. Moreno-Ancillo A, Martin-Munoz F, Martin-Barroso JA, et al. Anaphylaxis to 6-$\alpha$-methylprednisolone in an eight-year-old child. J Allergy Clin Immunol 1996;97:1169–1171.
43. Fernandez S, Reano M, Vives R, et al. 6-Methylprednisolone-induced bronchospasm. Allergy 1997;52:780–782.
44. Polosa R, Cacciola R, Pacino G, Prosperini G. Anaphylactic reaction to oral prednisone: a case report and review of the literature. Ann Ital Med Int 1998;13:47–52.
45. Beynel P, Guerin JC. Anaphylactic reactions to systemic corticosteroids. Review of the literature concerning 3 cases [in French]. Rev Mal Respir 1999;16:529–537.
46. Alexiou C, Kau RJ, Luppa P, Arnold W. Clinical significance of allergic reactions to glucocorticoid therapy [in German]. Laryngorhinootologie 1999;78:573–578.
47. Asakawa H, Araki T, Tsutsumi Y, Kawakami F. Skin tests of steroid allergy. Allergy 1999;54:645–646.
48. Escribano-Rodriguez MM, Gonzalez-Pol J, Munoz-Bellido FJ, et al. Immediate reaction to methylprednisolone with tolerance to other corticosteroids. Allergy 1997;52:677–678.
49. Schonwald S. Methylprednisolone anaphylaxis. Am J Emerg Med 1999;17:583–585.
50. Laine-Cessac P, Moshinaly H, Gouello JP, et al. Severe anaphylactoid reactions after intravenous corticosteroids. Report of a case and review of the literature [in French]. Therapie 1990;45:505–508.
51. Preuss L. Allergic reactions to systemic glucocorticoids: a review. Ann Allergy 1985;55:772–775.
52. Kamm GL, Hagmeyer KO. Allergic type reactions to corticosteroids. Ann Pharmacother 1999;33:451–460.
53. Bousquet J, Michel F. In vivo methods for study of allergy. Skin tests, techniques, and interpretation. In: Middleton E Jr, Reed CE, Ellis EF, et al, editors. Allergy: Principles and Practice, 4th ed. St. Louis: Mosby-Year Book, 1993:573–594.
54. Feigenbaum BA, Stevenson DD, Simon RA. Hydrocortisone sodium succinate does not cross-react with aspirin in aspirin-sensitive patients with asthma. J Allergy Clin Immunol 1995;96:545–548.
55. Szczeklik A, Nizankowska E, Czerniawska-Mysik G, Sek S. Hydrocortisone and airflow impairment in aspirin-induced asthma. J Allergy Clin Immunol 1985;76:530–536.
56. Stevenson RD, Simon RA. Sensitivity to aspirin and nonsteroidal antiinflammatory drugs. In: Middleton E Jr, Reed CE, Ellis EF, et al, editors. Allergy: Principles and Practice, 4th ed. St. Louis: Mosby-Year Book, 1993:1747–1765.
57. Daffern PJ, Muilenberg D, Hugli TE, Stevenson DD. Association of urinary leukotriene $E_4$ excretion during aspirin challenge with severity of respiratory symptoms. J Allergy Clin Immunol 1999;104:559–564.

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