ADRENAL SUPPRESSION FROM INTRADERMAL TRIAMCINOLONE*

A. DAVID McGUGAN, M.A., M.B.,** SAM SHUSTER, PH.D., M.B., B.S., M.R.C.P. AND EVA BOTTOMS, B.Sc.

Because of the extensive use of intralesional corticosteroids in the treatment of a wide variety of dermatological conditions, (1, 2), it was decided to investigate whether sufficient hormone was absorbed after intradermal injection to induce adrenal suppression; and if so, at what dose such suppression might occur, and for how long.

Methods

Eighteen patients, male and female, aged 17 to 72 years, were studied. All were in-patients, not confined to bed, with one of several dermatoses including psoriasis and atopic dermatitis. None had previously received corticosteroid therapy. Blood was drawn between 9 and 11 a.m. to minimize the effect of the diurnal variation in plasma cortisol concentration. The samples were heparinized and the plasma was separated and stored frozen until analyzed. After obtaining two control blood samples, 0.63 to 2.5 ml. of triamcinolone diacetate or triamcinolone acetonide tertiary butyl acetate containing 40 mg. per ml. was injected intradermally (in divided doses in volumes of 0.3 ml. or less) into normal skin on the lateral aspect of the thighs in 14 patients and intralesionally into psoriatic plaques on the limb and trunk in 4 patients. Further blood samples were obtained on the following four or five days.

Plasma cortisol was measured as free (unconjugated) 17 hydroxy-corticosteroid (17-OHCS) by the method of Peterson *et al.* (3) with slight modifications (4). Triamcinolone was used because the 16-OH group quenches the Porter-Silber reaction (4); thus triamcinolone and its metabolites are not measured by the present method. We could be certain, therefore, that all plasma-free 17-OHCS measured in this way was endogenous in origin.

Results

There was some fluctuation in the basal plasma cortisol concentrations before triamcinolone was injected, and several of the concentrations were at or below the lower range of normal for this method. This was technical in origin, due to high blank readings from interfering chromogens.

Five patients received 100 mg. and three patients 75 mg. of triamcinolone acetonide tertiary butyl acetate intradermally or intralesionally (figures 1 and 2). Plasma cortisol concentrations fell in all but one of these patients, in whom however blood was not obtained on the day after the injection (figure 1). The degree to which the plasma cortisol concentrations fell indicates virtually complete suppression of adrenal secretion of cortisol in six of the patients. By day six of the experiment, that is five days after injection of the triamcinolone, plasma cortisol concentrations had returned to normal in all but one of the patients.

Six patients received 50 mg. of triamcinolone acetonide tertiary butyl acetate and the plasma cortisol concentrations fell below normal in two of these, but was normal again on the next day (figure 3).

The four patients receiving 25 mg. of triamcinolone diacetate showed no significant depression of their plasma cortisol concentrations (figure 4).

The results in the four patients receiving intralesional triamcinolone derivatives were similar to those receiving intradermal injections into normal skin at the same concentration (figures 1–4).

Discussion

Our findings indicate that intradermal injections of triamcinolone derivatives can induce adrenal suppression. With doses of 50 mg. of triamcinolone acetonide tertiary butyl acetate, adrenal suppression was found only occasionally and was transient. By contrast, suppression was usual when 75–100 mg. of triamcinolone acetonide tertiary butyl acetate was injected and this suppression persisted in most patients for up to four days. This suggests that absorption of the steroid from the skin was correspondingly prolonged. In this respect the present results are similar to those found when triamcinolone was injected into the knee (5), when the possibility was considered that the prolonged adrenal suppression was due to slow absorption of corticosteroid bound by a component of the joint capsule. Prolonged absorption could also be due to insolubility of the steroid preparation (6).

The degree and duration of adrenal suppression induced by 75–100 mg. of triamcinolone acetonide tertiary butyl acetate is such that adrenal atrophy could be induced by repeated injections. Furthermore with doses of this order, the usual contraindications to corticosteroid therapy apply. The findings suggest that doses of triamcinolone diacetate of 25 mg. or less are unlikely to produce systemic effects.

* From the Institute of Dermatology, St. John's Hospital for Diseases of the Skin, Lisle Street, London, W.C. 2.

** Present address: 36, Adams Street, Quincy 69, Mass., U.S.A.

Received for publication February 11, 1963.

We are grateful to the Research Sub-Committee of the Institute of Dermatology for a grant to A.D.M. and to the Medical Research Council for a grant to S.S.

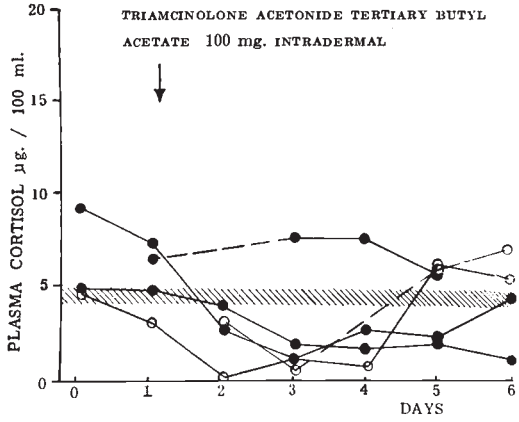

FIG. 1

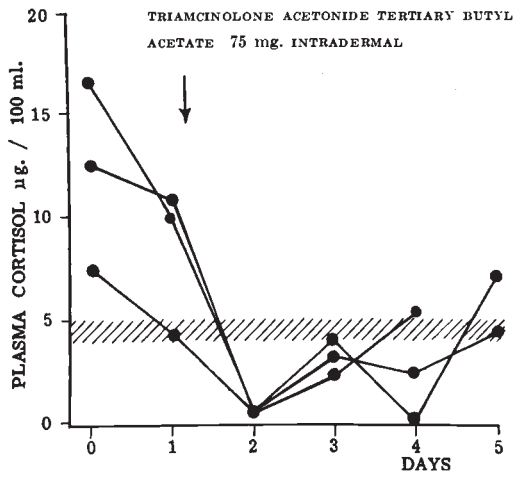

FIG. 2

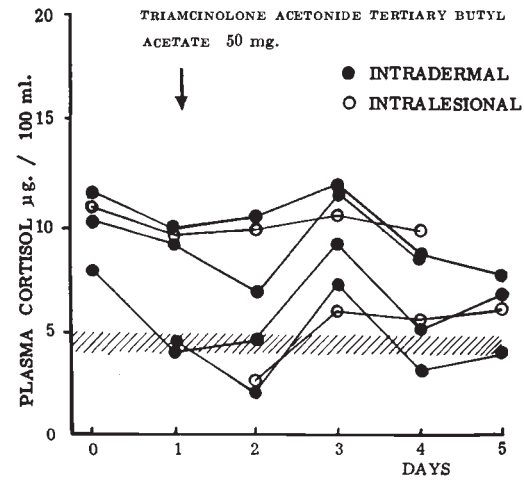

FIG. 3

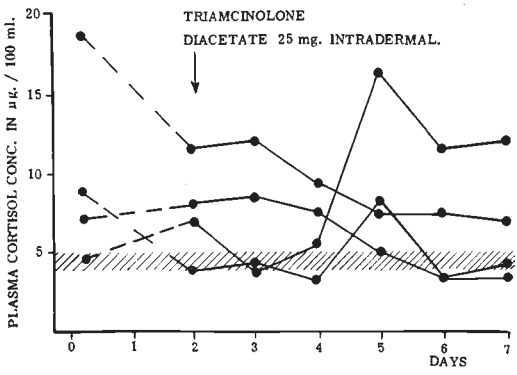

FIG. 4

FIGS. 1–3. Plasma cortisol concentrations before and after an injection of triamcinolone acetonide tertiary butyl acetate.
FIG. 4. Plasma cortisol concentrations before and after an injection of triamcinolone diacetate

Summary

A single injection of 75–100 mg. triamcinolone acetonide tertiary butyl acetate induced adrenal suppression as measured by a decrease in plasma cortisol concentration, which persisted up to four or more days. By contrast, with 25 mg. of triamcinolone diacetate, or 50 mg. of triamcinolone acetonide tertiary butyl acetate adrenal suppression was occasional and transient. It is concluded that 25 mg. or less of triamcinolone diacetate should be a safe dose for intralesional injection therapy.

REFERENCES

1. GUIN, JERE D., KNOX, JOHN M., CHERNOSKY, MARVIN E. AND SHAPIRO, EDWARD M.: Prednisolone acetate. A useful steroid preparation for intradermal administration. Arch. Derm. (Chicago), **81:** 438, 1960.
2. PELZIG, A. AND BAER, R.: Treatment of psoriasis with intralesional injection of triamcinolone. J. A. M. A., **173:** 898, 1960.
3. PETERSON, R. E., KARRER, A. AND GUERRA, S. L.: Evaluation of the Silber-Porter procedure for determination of plasma hydrocortisone. Anal. Chemistry, **29:** 144, 1957.
4. HATFIELD, C. B. AND SHUSTER, S.: The inhibitory effect of triamcinolone on adrenal function. J. Clin. Path., **12:** 140, 1959.
5. SHUSTER, S. AND WILLIAMS, I. A.: Adrenal suppression due to intraarticular corticosteroid therapy. Lancet, ii: 171, 1961.
6. GOLDMAN, L.: Histological effects of hydrocortisone in the skin of man. Ann. N.Y. Acad. Sci., **61:** 520, 1955.